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PERICARDITIS WITH EFFUSION FOLLOWING INFECTIONS OF THE UPPER RESPIRATORY TRACT

MAJOR DAVID A. NATHAN, M.C., AND
LIEUTENANT COLONEL RICHARD A. DATHE, M.C.

IN 1943 and 1944, eight patients with acute pericarditis with effusion were admitted to this Army installation. Our interest in these cases was stimulated by many basically similar features concerning the predisposing cause and seasonal incidence. The well-known etiological entities such as rheumatic fever, pneumonia (especially with empyema), pulmonary tuberculosis, and coronary thrombosis with myocardial infarction[1] were not considered likely in any of these cases.

The purpose of this report is to emphasize the relationship of apparently trivial and unimportant infections of the upper respiratory tract to pericarditis with effusion.

CASE REPORTS

CASE 1.—A 28-year-old white man was admitted to the hospital on March 11, 1944. The onset of his illness occurred approximately six weeks prior to admission when pain developed in the region of the sternum. This pain at times was very severe, practically continuous, and accentuated by deep breathing. It frequently was referred up to the neck and down the arms. Marching at double time and other exercise accentuated the pain. A "cold" and sore throat developed on or about Jan. 15, 1943.

There was no history of rheumatic fever, pneumonia, tuberculosis, or empyema. A tonsillectomy had been performed at the age of 6 years.

Physical Examination.—The breath sounds were slightly roughened at the left base, but there were no râles or other adventitious sounds. The blood pressure was 106/70. A prominent to-and-fro scratchy sound was heard over the entire precordium but was more prominent at the apex. The aortic and the pulmonic second sounds were clearly audible. The heart rate was 110 per minute.

Course.—The patient continued to complain of precordial pain for seven days after admission to the hospital. The pericardial friction rub was consistently present throughout this time. Frequent fluoroscopic studies revealed a gradual widening of the cardiac shadow to the right and left with absence of cardiac pulsations. On the seventh hospital day, a pericardiocentesis was performed, and 350 c.c. of reddish amber fluid were removed. Ninety cubic

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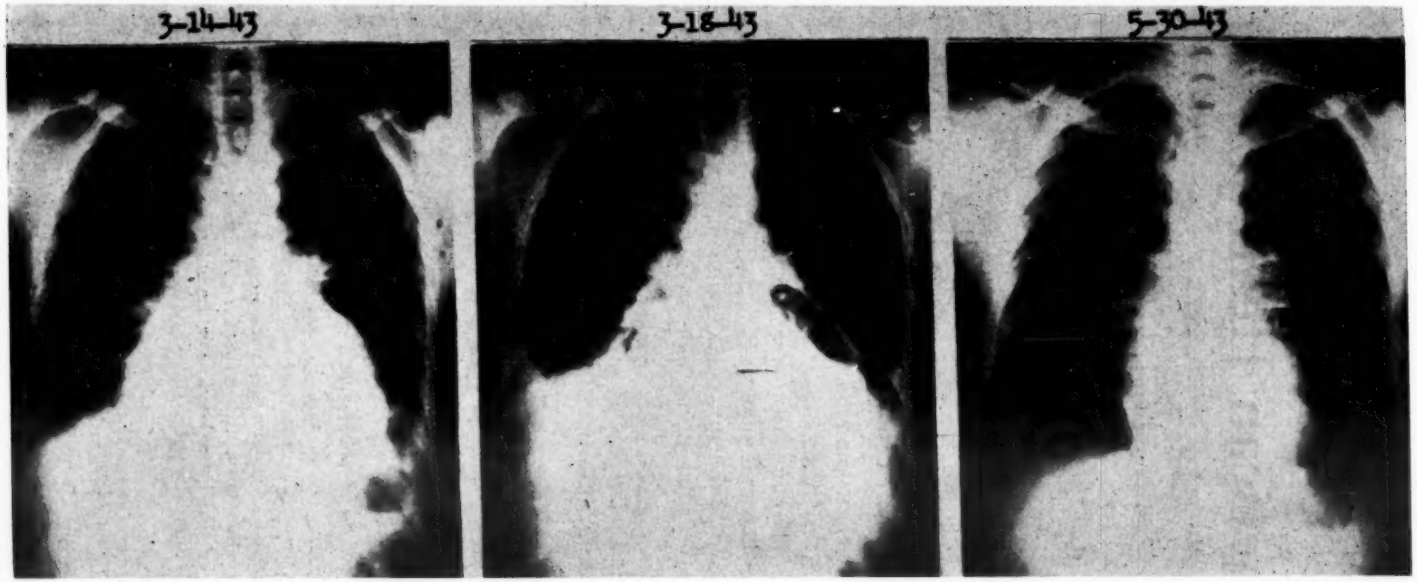

Fig. 1.—Case 1. Marked enlargement of cardiac shadow with subsequent return to normal. Note prominence of left cardiac border and obtuse right cardiodiaphragmatic angle. The film of March 18, 1943, was made following withdrawal of 350 c.c. of hemorrhagic fluid and injection of 90 c.c. of air.

centimeters of air were injected into the pericardial sac. Immediately after pericardiocentesis, metalic tinkles were heard, and the friction rub was prominent. The latter disappeared nine days later. The patient did well following this procedure, but there was a persistent tachycardia, varying from 100 to 130 per minute, while at rest in bed. The tachycardia gradually subsided, and the course of convalescence was essentially uneventful thereafter. The blood pressure was always between 100/70 and 120/80. The temperature was 102.2° F. on admission. There was a slight fluctuation between 99° and 102° F. for eight days and it was normal thereafter. The venous pressure was 10.5 cm. of blood on the fourth hospital day and rose to 20 cm. on the ninth hospital day. A total of 25 Gm. of sulfathiazole was given during the first week. Since there was no clinical improvement, the drug was discontinued.

Laboratory Findings.—The white blood cell count which was 16,400 per cubic millimeter on admission, rose to 27,400 on the seventh day, and gradually returned to normal. The differential count showed 85 to 95 per cent polymorphonuclear leucocytes. The red blood cell count was 4,250,000 per cubic millimeter with 85 per cent hemoglobin. The highest sedimentation rate was 27 mm. per hour. The sputum was negative for tubercle bacilli on three occasions. The blood serologic test was negative. The pericardial fluid contained a large number of red blood cells, occasional lymphocytes, and serosal cells. The stain and culture for acid-fast and nonspecific organisms were sterile. A guinea pig inoculation was negative for tuberculosis (Fig. 1).

X-Ray Examinations.—On March 14, 1943, the transverse cardiac diameter measured 15.7 centimeters. There was fullness and prominence of the left ventricle, and the right cardiodiaphragmatic angle was obtuse. The hilum shadows were accentuated, and there were heavy peribronchial vascular markings radiating into the lung field. The cardiothoracic ratio was 65 per cent. Following the pericardial tap, the heart size seemed to be within normal limits. The pericardium was well visualized and appeared to be considerably thickened. On May 30, 1943, the transverse diameter of the heart measured 12.2 cm. and was essentially normal in size and shape.

Electrocardiographic Findings.—On March 12, 1943, there was some straightening of the S-T segments in Leads I and II, but no significant elevation. The Q_3 measured 1½ mm., and T_3 was inverted. On March 29, 1943, the descending limb of T_1 was diphasic. The T_2 was inverted, and T_4 was isoelectric. On May 19, 1943, the T_1 was upright, T_2 was diphasic, and T_3 was inverted (Fig. 2).

CASE 2.—A 28-year-old white man was admitted to the hospital on March 13, 1943. About 3:00 A.M. on the day of admission, the patient was awakened with a severe pain in the chest and left upper abdomen. The pain was agonizing in character and made worse by deep inspiration or by attempting to lie flat in bed. Relief was obtained by sitting up and crouching forward. A sore throat was present five days prior to admission.

Physical Examination.—The patient was acutely ill, the skin was cold and clammy, and the blood pressure measured 110/70. There was a loud pericardial friction rub present over the entire precordium but most intense at the apex. The remainder of the physical examination was essentially negative.

Course.—The pericardial friction rub remained for about twelve hours after admission. The liver became palpable after twenty-four hours and was slightly tender. The temperature varied from normal to 102° F. for about two weeks, after which a low-grade fever to 99.6° F. persisted until the fifth week of illness. The liver remained palpable for several weeks. Convalescence was slow but finally complete.

X-Ray and Fluoroscopic Examinations.—On March 14, 1945, the heart was symmetrically enlarged in all directions with encroachment on the posterior clear space. Fluoroscopy revealed feeble cardiac pulsations on admission with progressive improvement in the amplitude of the ventricular systole as the patient improved.

Electrocardiographic Findings.—On March 13, 1944, there was an elevation of the S-T segments in Leads I and II of 1 and 2 mm., respectively. The S-T_4 was straight. On March 15, 1944, there was a slight increase in the elevation of the S-T_1 and the S-T_2. On March 22, 1944, the descending limbs of T_1 and T_2 showed a diphasic tendency. By March 29, 1944, T_1,

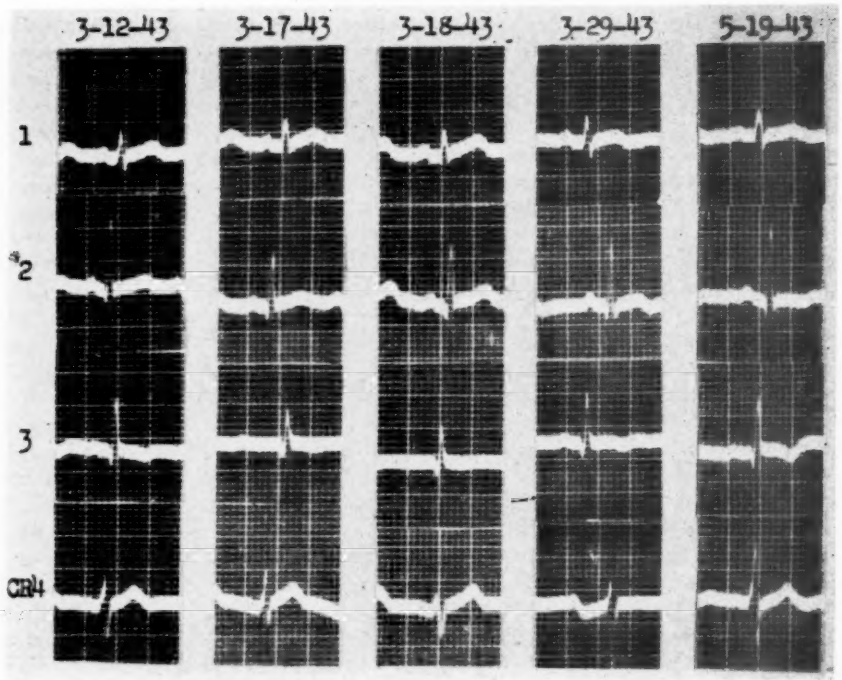

Fig. 2.—Case 1. There is progressive inversion of the T waves in all leads with somewhat straightened and elevated S-T segments particularly in Leads I and II. (Lead CR_4 taken on March 29, 1943, is upside down.)

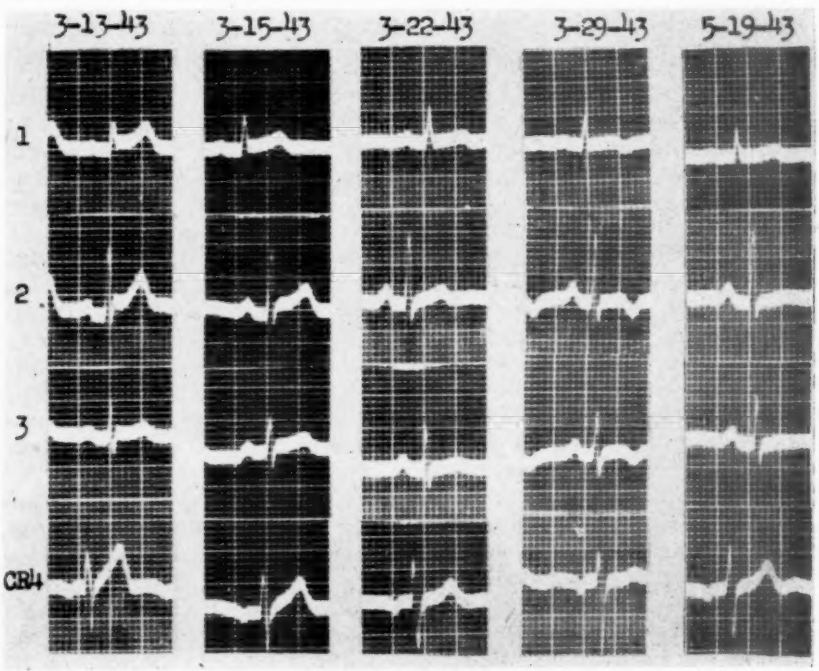

Fig. 3.—Case 2. There is high take-off of ST_1 segments in the electrocardiogram taken on March 13, 1944. This is followed by progressive inversion of the T waves and subsequent return to normal.

T_2, and T_3 were inverted. An electrocardiogram taken on May 19, 1944, was essentially normal except for the low voltage of T_2 and an isoelectric T_3 (Fig. 3).

CASE 3.—A 21-year-old white man was admitted to the hospital on July 20, 1943. He became ill on June 11, 1943, with acute nasopharyngitis, at which time he was admitted to the hospital and treated with a total of 28 Gm. of sulfathiazole. The recovery was uneventful. The chest was negative at the time of discharge from the hospital on July 2, 1943. On readmission, he complained of severe, substernal pain which was aggravated by the slightest motion and by deep inspiration. On the first hospital day, the patient was acutely ill with a temperature of 102° F. and a mild cyanosis of the lips and fingernails. The severe pain in the chest persisted and spread to the left side. Nineteen days after admission, fluid developed in the left thorax. Four hundred cubic centimeters of slightly cloudy amber fluid were removed. The precordial pain persisted, although no pericardial friction rub was heard. There was gradual decrease in the size of the heart, and the patient made an uneventful recovery. The temperature fluctuated from 100° to 102.2° F. several days before returning to normal.

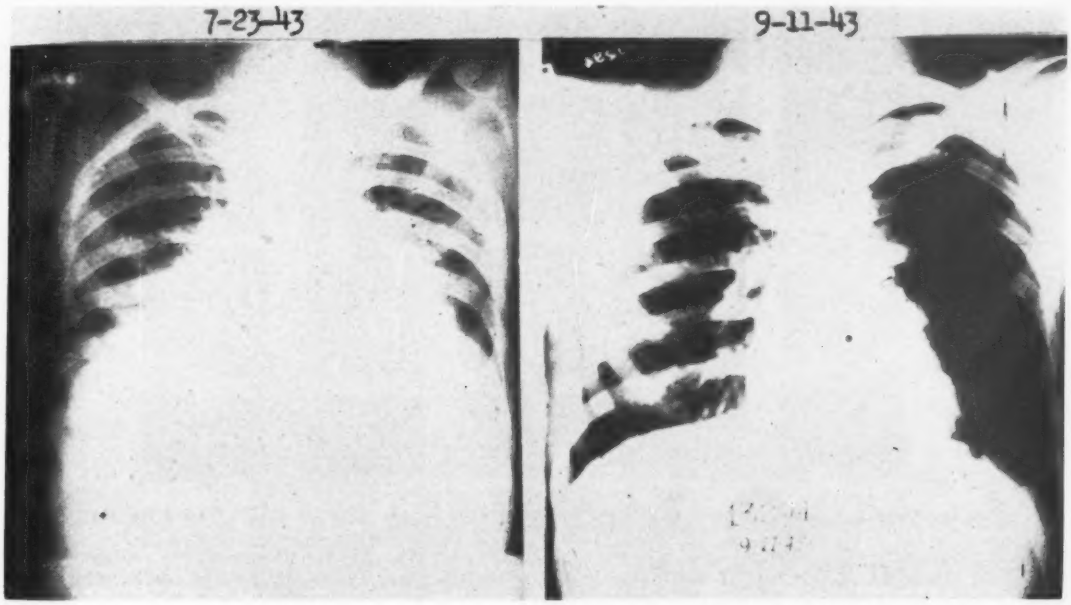

Fig. 4.—Case 3. Marked enlargement of the cardiac shadow and return to normal. The cardiodiaphragmatic angles are obscured by marked congestive changes in the film taken on July 23, 1943.

Laboratory Findings.—The white blood cell count was 12,000 per cubic millimeter with 79 per cent polymorphonuclear leucocytes and 17 per cent lymphocytes. The red blood cell count was 4,940,000 cubic millimeters with 94 per cent hemoglobin. The leucocyte count rose to 22,600 on the sixth hospital day and gradually returned to normal. The nonprotein nitrogen of the blood was 48.4 mg. per cent. The blood culture was sterile. The highest sedimentation rate was 8 mm. per hour. The pleural fluid had a specific gravity of 1.015 with 3,200 white blood cells per cubic millimeter. The differential count of the pleural fluid showed 85 per cent lymphocytes and 14 per cent polymorphonuclear leucocytes. The stained film, culture, and guinea pig inoculation showed no evidence of tuberculosis after eight weeks.

X-Ray and Fluoroscopic Examinations.—On July 23, 1945, the transverse cardiac diameter measured 16.1 centimeters. The left border of the heart was somewhat convex in the region of the left auricle and the pulmonary conus. The cardiodiaphragmatic angles were not clearly defined. Evidence of congestive changes in both hilar regions was present.

Fluoroscopy revealed a very slight pulsation of the left ventricular systole. On Sept. 11, 1943, the transverse cardiac diameter measured 12.3 centimeters. The heart and lung fields were within normal limits (Fig. 4).

Electrocardiographic Findings.—On July 21, 1943, there was straightening of the S-T segments in Leads I and II with slight elevation of S-T_1 and S-T_2. There was a gradual reversal of the axis of T_1 and T_2 to negativity by Aug. 10, 1943. On Oct. 20, 1943, T_1 was still low in voltage (Fig. 5).

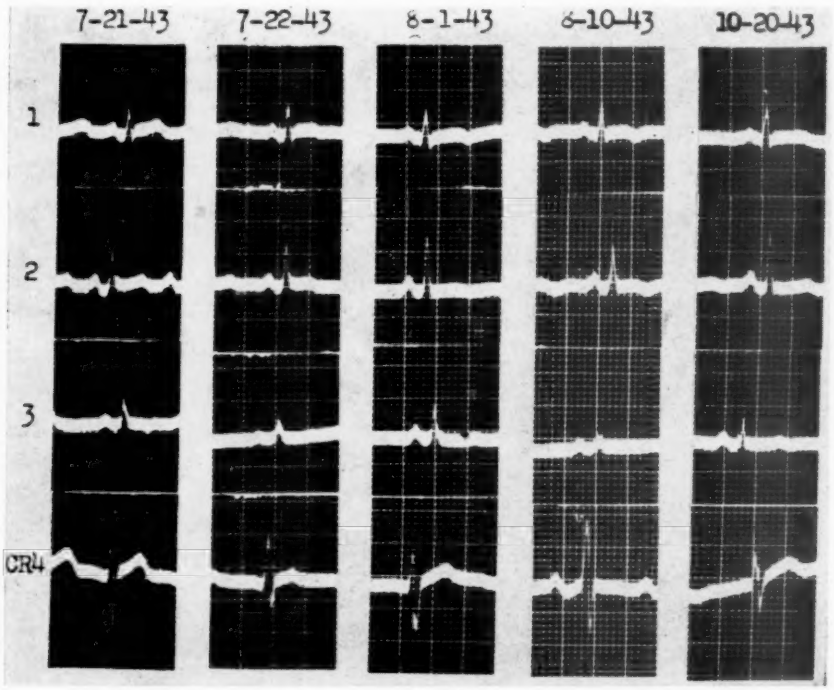

Fig. 5.—Case 3. Early changes consist of straightening and elevation of ST_1 and ST_2; later there is inversion of the T waves in Leads I and II.

CASE 4.—A 36-year-old white man was admitted to the hospital on Sept. 13, 1943. The onset of the illness occurred about two weeks prior to admission when substernal pain developed. The pain started after arising from bed and became progressively worse during the day. He was forced to take shallow breaths and flex his body forward to relieve the pain. The patient stated that he felt as if his chest was being torn away. There was some referred pain to the neck, shoulders, and arms. The previous personal history was essentially negative except for typhoid fever in 1925.

Physical Examination.—The blood pressure was 128/75. There was a moderately low-pitched to-and-fro scratchy roughened sound just to the left of the xiphoid. No murmurs were present. The remainder of the physical examination was essentially negative.

Course.—The pericardial friction rub was present for twelve days after admission. Three days after admission a pericardial aspiration was done, and 50 c.c. of hemorrhagic fluid were removed. The clinical course was uneventful thereafter, and the patient was discharged from the hospital on Nov. 8, 1943.

Laboratory Findings.—The highest white blood cell count was 11,000 per cubic millimeter. The erythrocytes numbered 4,900,000 per cubic millimeter with 85 per cent hemoglobin. The differential counts were within normal limits. The highest sedimentation rate was 24 mm. per hour. The pericardial fluid was hemorrhagic with a hematocrit of 10. Micro-

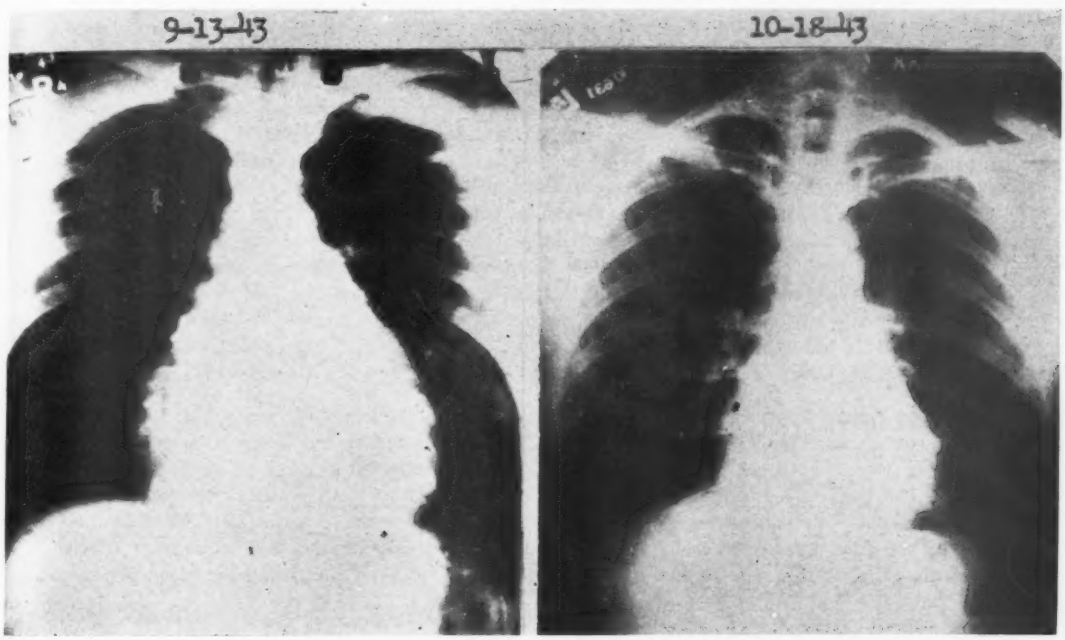

Fig. 6.—Case 4. Note "water bottle" configuration of the heart in the film taken on Sept. 13, 1943, and subsequent return to normal.

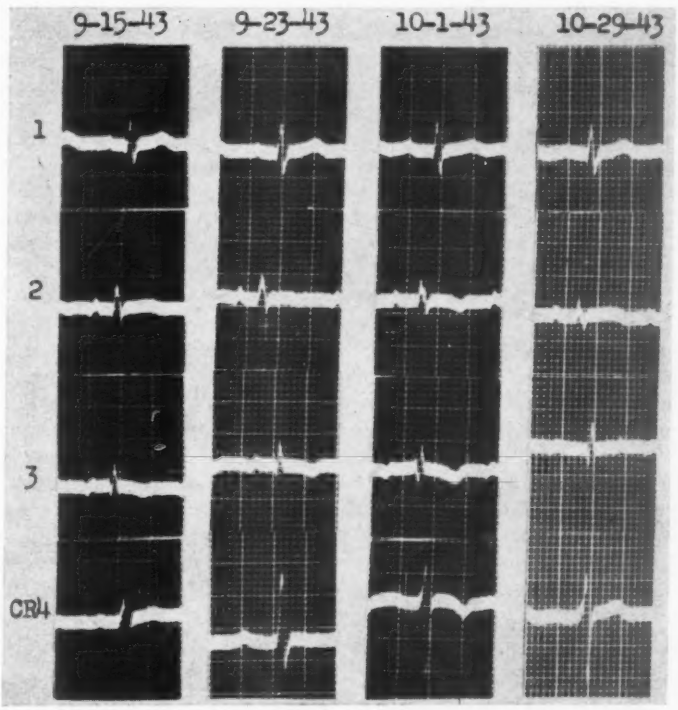

Fig. 7.—Case 4. The most marked changes consist of progressive inversion of the T waves in Leads II, III, and IV.

scopic examination showed laked red blood cells, a few polymorphonuclear leucocytes, and an occasional monocyte. The film and culture were sterile. The inoculated guinea pig was negative for tuberculosis.

X-Ray and Fluoroscopic Examinations.—On Sept. 13, 1943, the transverse cardiac diameter was 19.5 centimeters. There was a "water bottle" configuration of the cardiac shadow with fullness of both lower heart borders and straightening of the left cardiac waistline. The cardiothoracic ratio was 19.5:31.5 centimeters. The lung fields were essentially clear except for some generalized accentuation of the bronchovascular markings (Fig. 6). Fluoroscopy revealed feeble cardiac pulsations along the left cardiac border and some fullness posteriorly in the left oblique position. Considerable broadening of the supercardiac shadow was noted in the Trendelenburg position. On Oct. 18, 1943, the heart and lung fields were essentially normal. The transverse cardiac diameter measured 13.4 cm. (Fig. 7).

Electrocardiographic Findings.—On Sept. 15, 1943, the T_2 and T_4 waves showed low voltage, and T_3 was slightly inverted. Thereafter T_2, T_3, and T_4 showed progressive inversion. On Oct. 29, 1943, the descending limb of T_2 was diphasic, and the voltage of T_3 was low.

CASE 5.—A 32-year-old white man was admitted to the hospital on Jan. 18, 1944. One week prior to admission he developed a "cold" and sore throat followed by substernal pain which was severe at times and accentuated by cough, by deep inspiration, or by motion of the body. The pain lasted three or four days. The past history was essentially negative.

Physical Examination.—The apex of the heart was percussed 11 cm. from the midsternal line in the fifth intercostal space. The sounds were slightly distant, but no murmurs were present. The rhythm was regular, the heart rate was 100 per minute, and the blood pressure was 120/75.

Course.—Nine days after admission a pericardiocentesis was performed and 175 c.c. of hemorrhagic fluid were removed. Seventy-five cubic centimeters of air were injected into the pericardial sac. Much fluid remained, however, after this aspiration. On the twelfth hospital day a friction rub was heard over the xiphoid and at the base of the heart in the midsternal line. It was present for six days. Fluoroscopy of the heart showed almost complete refilling of the pericardial sac with complete resorption of air. There was progressive diminution of the heart shadow thereafter, and the pulsations gradually increased in force and amplitude. The patient was discharged to furlough on May 6, 1944. Upon returning, there was a recrudescence of symptoms. Fluoroscopy of the heart showed a recurrent pericardial effusion. Spontaneous subsidence of this phase of illness occurred twenty-seven days later.

Laboratory Findings.—The highest white blood cell count was 8,500 per cubic millimeter with an essentially normal differential count. The erythrocytes numbered 4,150,000 per cubic millimeter with 85 per cent hemoglobin. The highest sedimentation rate was 21 mm. per hour. The pericardial fluid was hemorrhagic with a hematocrit of 6. The fluid contained mostly lymphocytes, many red blood cells, and an occasional polymorphonuclear leucocyte. The slide film and culture of the fluid were negative. A guinea pig inoculation with the fluid was negative for tuberculosis.

X-Ray Findings.—On Jan. 25, 1944, the transverse cardiac diameter measured 18.3 centimeters. The heart was globular in shape. The hilum markings were accentuated. On Jan. 28, 1944, after pericardiocentesis, there was a moderate amount of air in the pericardial sac along the left heart border. Moderate accentuation of the hilum markings persisted. On June 28, 1944, the transverse cardiac diameter measured 14.4 centimeters. The heart was essentially normal, although accentuation of the right hilum shadow was still evident (Fig. 8).

Electrocardiograhpic Findings.—On Jan. 22, 1944, there was slight elevation of the S-T segments in Leads I and II. On Feb. 3, 1944, T_1 was inverted. The S-T_2 was straight with an elevation of 1 millimeter. On Feb. 26, 1944, T_1 was low in voltage but upright. T_2 and T_3 were inverted. On April 10, 1944, the electrocardiogram was essentially normal (Fig. 9).

CASE 6.—A 31-year-old white man was admitted to the hospital on Jan. 20, 1944. He was well until forty-five days before admission, when he developed malaise, fever, slight cough, and vague fleeting chest pains. In the latter part of November, 1943, he developed a "cold" which did not subside. On Dec. 25, 1943, he was seized with severe substernal pain which did

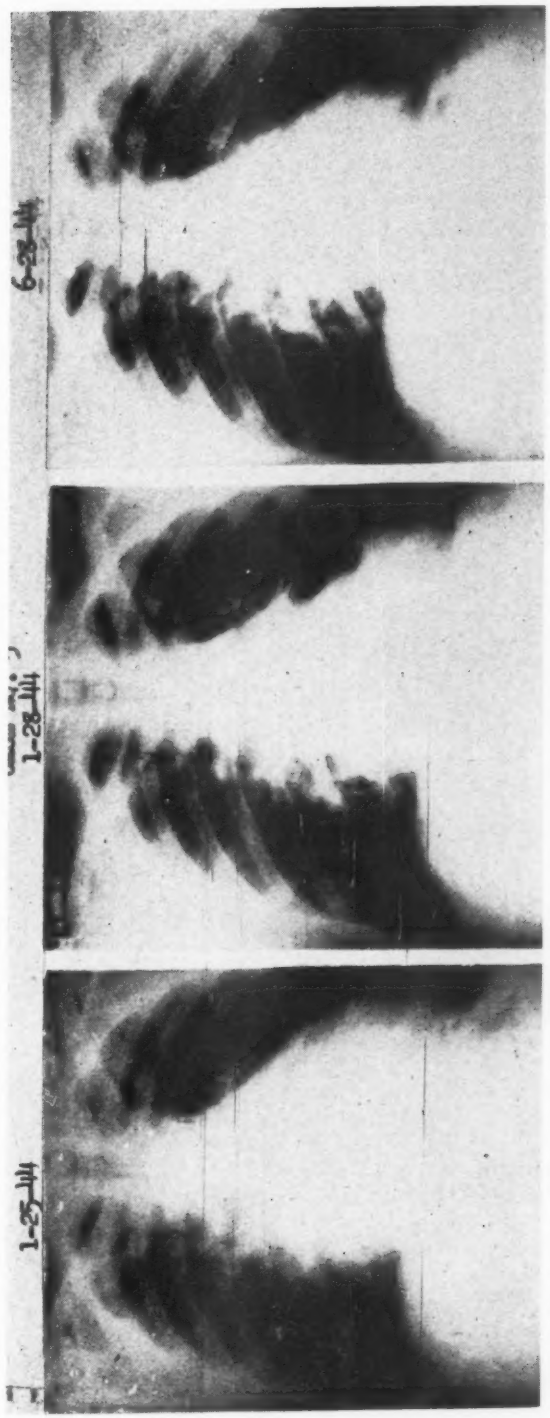

Fig. 8.—Case 5. The cardiodiaphragmatic angles remain acute although marked pericardial effusion is present. This x-ray was made on Jan. 28, 1944, after aspiration of 175 c.c. of hemorrhagic fluid and injection of 75 c.c. of air into the pericardial sac.

not radiate. It was aggravated by inspiration or motion. The pain was frequently relieved by sitting forward. There was a loss of 15 pounds of weight prior to hospitalization. The past history was essentially negative.

Physical Examination.—The heart sounds were somewhat muffled, but otherwise not remarkable. There was no pericardial friction rub. The liver was palpable 4 cm. below the costal margin in the anterior axillary line. The remainder of the physical examination was essentially negative. The blood pressure was 115/90.

Course.—The patient was observed until Feb. 24, 1944, when he was transferred to a general hospital. There was gradual improvement, although the liver remained palpable and slightly tender. After the fourteenth hospital day, the muffled heart sounds disappeared. Thereafter, the sounds were essentially normal.

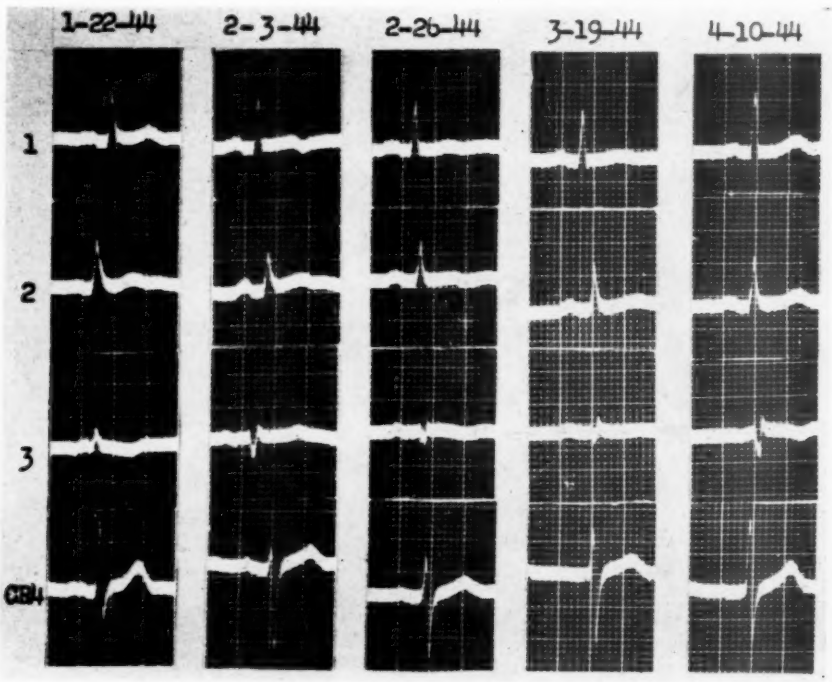

Fig. 9.—Case 5. There is progressive inversion of T_1 and T_2 in the first two tracings with subsequent return to normal.

Laboratory Findings.—The leucocyte count was 12,400 per cubic millimeter on admission with an essentially normal differential count. The erythrocytes numbered 4,500,000 per cubic millimeter with 95 per cent hemoglobin. The sedimentation rate was 15 mm. per hour on admission and remained at that level throughout his illness.

X-Ray and Fluoroscopic Examinations.—On Jan. 29, 1944, there was symmetrical enlargement of the heart with fullness of the left cardiac border. The transverse diameter of the heart measured 16.5 centimeters. The cardiothoracic ratio was 0.65. On Feb. 15, 1944, there was regression of the heart size to normal limits. Routine fluoroscopic examination revealed an absence of cardiac pulsations during the first fourteen days of hospitalization with subsequent return to normal pulsations thereafter.

Electrocardiographic Findings.—On Jan. 5, 1944, fifteen days prior to admission, an electrocardiogram was essentially negative. Seven days after admission, Jan. 27, 1944, T_1 was slightly inverted while T_2 and T_3 were inverted. There were notching and low voltage of T_4. On Jan. 31, 1944, the T waves were inverted in the limb leads while T_4 showed notching.

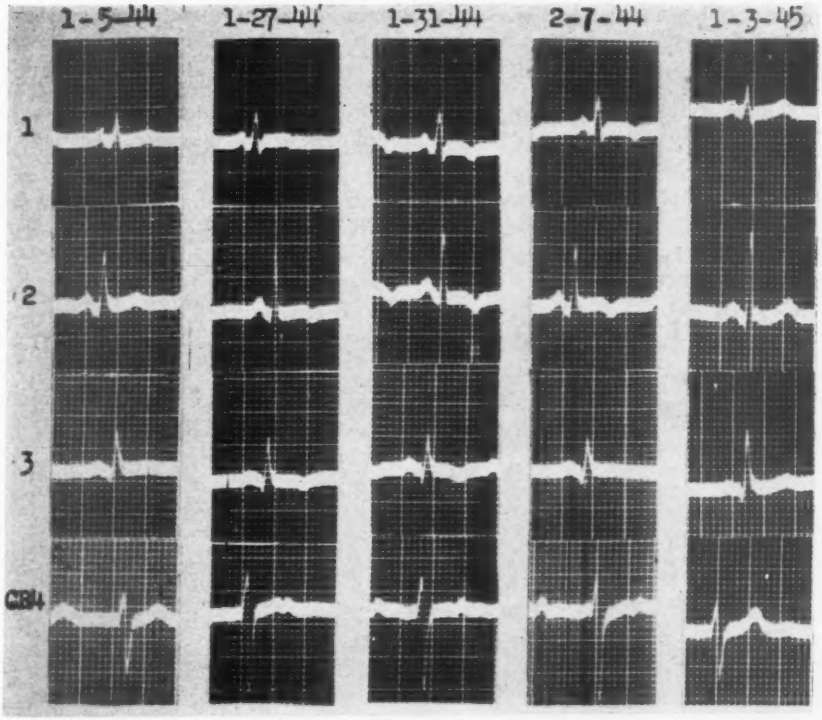

Fig. 10.—Case 6. There is progressive inversion of the T waves in all leads. Electrocardiogram of Jan. 3, 1945, was taken after complete clinical recovery.

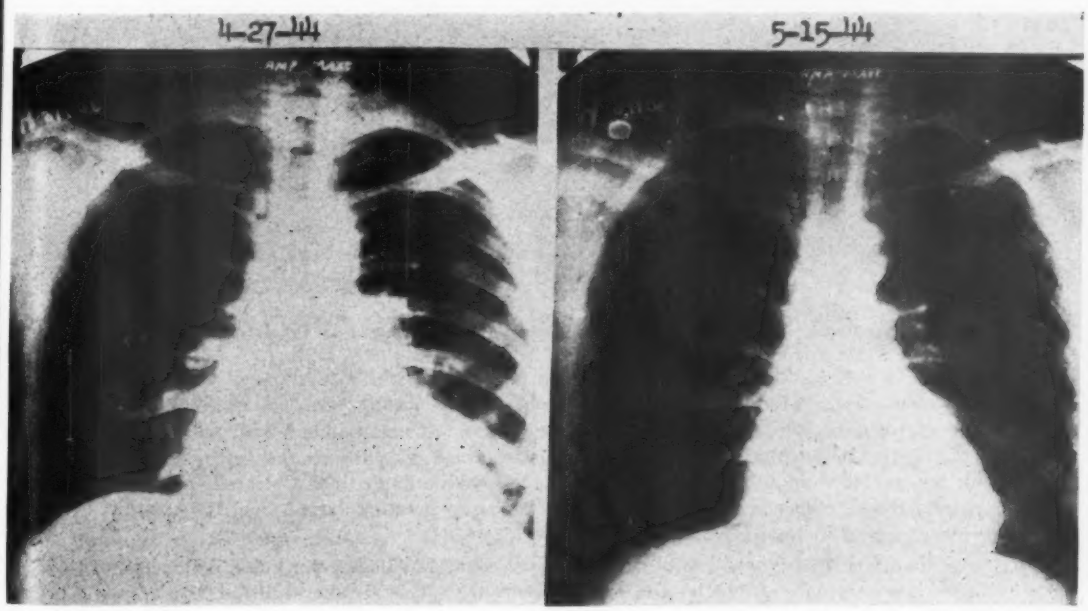

Fig. 11.—Case 7. There is moderate enlargement of the cardiac shadow with subsequent return to normal.

There was little improvement on Feb. 7, 1944, but on Jan. 3, 1945, the electrocardiogram was normal (Fig. 10).

CASE 7.—A 22-year-old white man was admitted to the hospital on April 26, 1944, with fever and chills of three days' duration associated with severe, substernal pain aggravated by deep inspiration. He had had a sore throat fourteen days before admission. The past history was essentially negative.

Physical Examination.—The patient was acutely ill with slight cyanosis of the face and lips. The heart was essentially normal except for a tachycardia of 120 per minute. The blood pressure was 125/70.

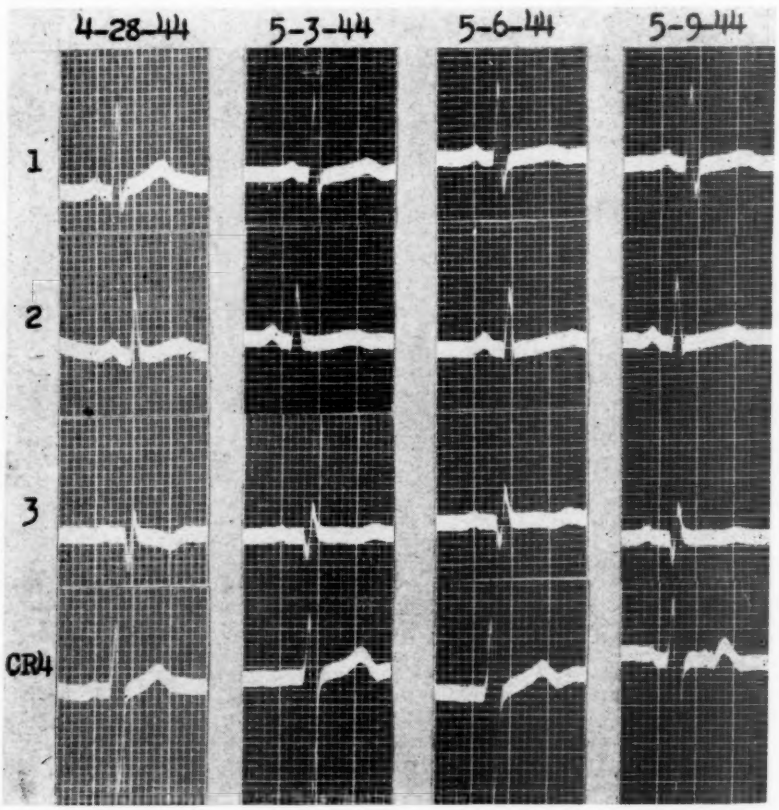

Fig. 12.—Case 7. There is a progressive decrease in the voltage of T_1 and T_2. Note straightened S-T segments in Leads I and II of electrocardiograms taken on May 6, 1944, and May 9, 1944.

Course.—Soon after admission the precordial pain disappeared. A pericardiocentesis was performed two days after admission, and 10 c.c. of clear amber fluid were removed. On the eleventh hospital day, the patient complained of pain in the left chest, and a small amount of fluid was found at the left costophrenic angle. This cleared within a few days, and the subsequent course was uneventful. The temperature varied from 100° to 102° F. for five days and was normal thereafter.

Laboratory Findings.—The highest leucocyte count was 20,600 per cubic millimeter with 92 per cent neutrophiles and 80 per cent lymphocytes. The highest sedimentation rate was 25 mm. per hour. The urinalysis was negative. The pericardial fluid showed a cell count of 1,000 per cubic millimeter with 96 per cent polymorphonuclear leucocytes and 4 per cent

lymphocytes. The slide film and culture of the fluid were essentially negative. Guinea pig inoculation with fluid was negative for tuberculosis (Fig. 11).

X-Ray and Fluoroscopic Examinations.—On April 27, 1944, the heart was enlarged to the left with no characteristic changes in contour. The transverse cardiac diameter measured 17.3 centimeters. The cardiothoracic ratio was 0.56. The lung fields were clear. On fluoroscopy, markedly diminished pulsations were present, and a posterior bulge of the pericardium was noted in the left oblique and lateral views. On May 15, 1944, the heart was normal in size and shape. The transverse cardiac diameter measured 14.7 centimeters.

Electrocardiographic Findings.—On April 28, 1944, Q_3 measured 3.5 millimeters. T_3 was inverted; S-T_1 was slightly straighter than usual. On May 3, 1944, there was a decrease in the voltage of T_1 and T_2. T_3 was less inverted, and then measured 2 millimeters. On May 6, 1944, there was a low voltage of T_1 and T_2 with straightening of the S-T segments in Lead II. On May 9, 1944, there was no change in the electrocardiogram (Fig. 12).

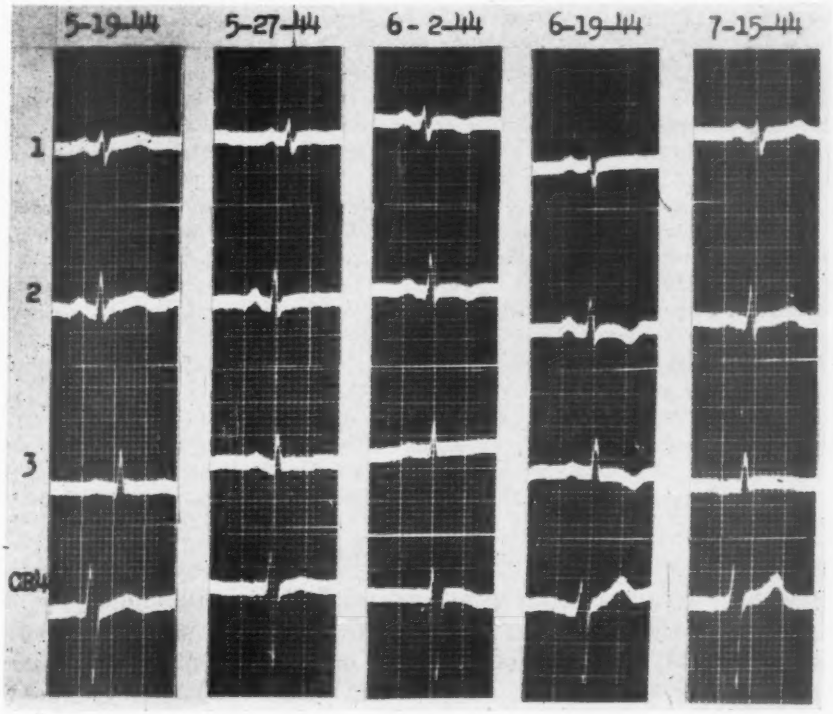

Fig. 13.—Case 8. There is progressive inversion of the T waves in all leads. Electrocardiogram of July 15, 1944, was taken after complete clinical recovery.

CASE 8.—A 33-year-old white man was admitted to the hospital on May 14, 1944. He became ill about four days prior to admission with substernal pain accentuated by deep inspiration and change of position particularly when recumbent. There was no definite history of an upper respiratory infection, although cough was present at the onset. The pain subsided slightly before admission to the hospital.

Past History.—He had had measles, mumps, and chicken pox in childhood. An appendectomy was performed in 1933. There were gonorrheal infections in 1936 and 1937. There was no history of rheumatic fever or tuberculosis.

Physical Examination.—There was a to-and-fro pericardial friction rub heard over the sternum at the level of the fourth rib in the midsternal line. The remainder of the physical examination was essentially negative.

Course.—A pericardiocentesis was done on May 25, 1944, and 3 c.c. of hemorrhagic fluid was obtained. This was repeated the next day, and 40 c.c. of similar fluid was recovered. A pericardial friction rub was present the first seventeen days of illness. Thereafter, the substernal pain disappeared, and the cardiac shadow receded to normal size. On the thirty-fourth hospital day, there was a recrudescence of fever and substernal pain. A friction rub was again heard over the left sternal border. The liver was felt 1 fingerbreadth below the costal margin in the anterior axillary line. Five days later the pericardial friction rub disappeared; the symptoms subsided, and recovery was uneventful.

Laboratory Findings.—The highest leucocyte count was 6,000 per cubic millimeter with 64 per cent neutrophiles, 22 per cent lymphocytes, 10 per cent monocytes, and 4 per cent eosinophiles. The white blood cell count varied between 6,000 and 3,800 per cubic millimeter. The erythrocytes numbered 4,400,000 per cubic millimeter with 85 per cent hemoglobin. The serologic test for syphilis was negative. The highest sedimentation rate was 20 mm. per hour. The pericardial fluid contained 695,000 red blood cells per cubic millimeter with a hematocrit of 6. There was evidence of old hemolysis. The slide film and culture of the fluid were negative. Guinea pig inoculation with the fluid was negative for tuberculosis.

X-Ray and Fluoroscopic Examinations.—On May 19, 1944, the heart was quite large with fullness of both lower cardiac borders and in the region of the pulmonary conus. On May 25, 1944, fluoroscopy showed diffuse enlargement of the heart shadow to the right and left with marked diminution in the amplitude of the ventricular systole. In the lateral view there was prominent bulging posteriorly. In the Trendelenburg position, the retrosternal width increased about 2 centimeters. On May 27, 1944, after pericardiocentesis, there was a small amount of air visible along the left border of the heart. On May 31, 1944, fluoroscopy showed a uniform enlargement of the cardiac shadow in all views with marked diminution in all pulsations. On June 13, 1944, there was a slight prominence of the pulmonary conus but no evidence of pericardial effusion. The heart was essentially normal. Subsequent x-ray films taken on July 12, July 19, and July 24, 1944, showed the heart to be normal in size.

Electrocardiographic Findings.—On May 19, 1944, there was slight elevation and straightening of the S-T segments in Leads I and II. T_3 was isoelectric. On May 27, 1944, T_1 was isoelectric. T_2 showed low voltage; T_3 was diphasic. On June 2, 1944, the T waves were inverted in Leads I and II; T_4 was slightly inverted. On June 19, 1944, T_1 was upright but low in voltage. T_2 and T_3 were markedly inverted with slight depression of S-T_2 and S-T_3. T_4 was upright. On July 15, 1944, the electrocardiogram was essentially normal (Fig. 13).

REVIEW OF CASES

Seven of the eight patients were admitted to the hospital during the months of high respiratory incidence (Table I). In case 3 the patient was admitted during July, 1943, but there was a history of acute nasopharyngitis nine days before admission. In six cases there was an unequivocal history of tonsillitis, pharyngitis, or nasopharyngitis. Two patients (Cases 4 and 8) had a nonproductive cough but no history of an antecedent upper respiratory infection.

Evidence of our diagnoses was manifested by a pericardial friction rub in five cases associated with severe substernal pain which was the initial complaint in each. The highest leucocyte counts varied from 6,000 to 27,400 per cubic millimeter. In five of eight cases, x-ray films were available for mensuration, while films in Cases 2 and 8 were not obtainable from the Veterans' Administration files. The measurement of the transverse cardiac diameter was possible in one original x-ray film in Case 1. Significant recession of cardiopericardial shadow is demonstrated in the illustrations in Cases 1, 3, 4, 5, and 7. Pericardiocentesis was performed in five cases. The fluid was hemorrhagic in four patients and clear amber in one. The red blood cells were hemolyzed, and

TABLE I. SUMMARY OF CASES OF PERICARDITIS WITH EFFUSION

CASE	DATE OF ADMISSION	RESPIRATORY INFECTION	PRECORDIAL FRICTION RUB	SUBSTERNAL PAIN	LEUCOCYTES (PER CU. MM.)	HEART DIAMETER (CM.)	PERICARDIAL FLUID	
							SEDIMENT	FILM CULTURE GUINEA PIG
1	3/11/43	Yes	Yes	++++	27,400	15.7	Reddish amber; laked R.B.C.; occasional lymphocytes and serosal cells	0
2	3/13/43	Yes	Yes	++++			No	
3	7/20/43	Yes	No	++++	22,600	16.1 12.3	No	
4	9/13/43	No (Cough)	Yes	++++	11,000	19.5 13.4	Hemorrhagic fluid; laked R.B.C.; hematocrit 10; few polys; occasional monocytes	0
5	1/18/44	Yes	Yes	++++	8,500	18.3 14.4	Hemorrhagic fluid; laked R.B.C., lymphs, and occasional polys; hematocrit 6	0
6	1/20/44	Yes	No	++++	12,400	16.5	No	
7	4/26/44	Yes	No	++++	20,600	17.3 14.7	Clear yellow fluid; cell count 1,000 per cubic millimeter with 96 per cent polys; 4 per cent lymphs	0
8	5/14/44	No (Cough)	Yes	++++	6,000		Hemorrhagic fluid; laked R.B.C.; R.B.C. count 695,000; hematocrit 6	0

the hematocrit varied from 6 to 10. Slide film, culture, and guinea pig inoculation of the pericardial fluid were negative for bacteria in all cases.

The commonest change in the electrocardiograms was a progressive inversion of the T waves, straightening of the S-T segments in seven cases, and the elevation of the S-T segments (0.5 to 2 mm.) in five cases.

COMMENT

Reports concerning the association of acute pericarditis with effusion to upper respiratory infections are not numerous. Willius[2] reported a single case of acute serofibrinous pericarditis following acute pharyngitis which he believed is a common form of pericarditis. The nature of the infecting organism was thought to be a streptococcus invading the pericardium. Levine[3] referred to a type of pericardial effusion due to a streptococcus infection but the effusion, however, was purulent. He considered the clinical condition a part of a generalized streptococcal infection which was associated especially with an antecedent sore throat. He also considered a virus infection as a possible etiological factor which does not produce empyema, shows no stigma of rheumatism, but resembles acute coronary occlusion. Wolff[4] reported five cases of pericarditis during an acute upper respiratory infection. Three cases were associated with atypical pneumonia.

In considering the pathogenesis of this condition in this series, two possibilities are considered: (1) The proximity of the hilum lymph nodes with extension of the infection into the pericardial sac. (2) A hypersensitive response by the pericardium to an offending organism in which the immune reaction of

the body is inadequate. This parallels the present accepted explanation of a hypersensitive reaction on the part of the heart and serosal linings of the joints in the rheumatic fever state.

The latter concept seems more plausible because the pericardial fluid was sterile and nonpurulent in the five cases in which pericardiocentesis was performed. A virus as the cause is not seriously entertained in this series since the leucocyte counts ranged as high as 27,400 per cubic millimeter.

The reports of necropsy records concerning pericarditis reveal interesting figures relative to the incidence of the disease. Smith and Willius,[5] reviewing 8,912 cases from the necropsy records of the Mayo Clinic, found 373 cases of pericarditis, or an incidence of 4.2 per cent from all causes. Seventy-one cases, or 49.3 per cent of 144 cases of adherent pericarditis, were of unknown etiology. They referred to the possibility that acute fibrinous pericarditis may take place as a result of an apparently trivial infection, which is not recognized at the time of occurrence and which may undergo spontaneous abatement, resulting in partial or complete obliteration of the pericardial sac. This is borne out by the fact that only 57 cases, or 39.5 per cent of their series, presented complaints that made the heart a major factor in the clinical picture. It is possible in the light of our series that an antecedent upper respiratory infection of mild or subclinical type may have been the etiological factor in some of their cases. Since in two of our cases a history of upper respiratory infection was not obtained, a subclinical antecedent carrier state may have existed, such as we now believe to be possible in many patients with rheumatic fever. If the preceding facts are true, clinical evaluation of mild or moderate precordial pain following in the wake of an acute upper respiratory infection takes on important clinical significance in that the symptoms may be due to a mild acute pericarditis.

Hard and fast conclusions cannot be made from this small series of cases, but it might be inferred that an antecedent upper respiratory infection without intrapulmonary disease may be an important predisposing cause of pericarditis with effusion.

SUMMARY

1. Eight cases of pericarditis with effusion following acute upper respiratory infection without intrathoracic disease are presented.

2. The relationship of acute upper respiratory infection of mild or subclinical type to partial or complete obliterative pericarditis found at autopsy is suggested.

REFERENCES

1. Cecil, R. L.: Textbook of Medicine, ed. 5, Philadelphia, 1940, W. B. Saunders Co., p. 1131.
2. Willius, F. A.: Cardiac Clinics, St. Louis, 1941, The C. V. Mosby Co., p. 30.
3. Levine, S. A.: Clinical Heart Disease, ed. 3, Philadelphia, 1945, W. B. Saunders Co., p. 64.
4. Wolff, L.: New England J. Med. 229: 423, 1943.
5. Smith, H. L., and Willius, F. A.: Arch. Int. Med. 50: 410, 1932.

HEMIPLEGIA FOLLOWING CAROTID SINUS STIMULATION

JOHN MARTIN ASKEY, M.D.
LOS ANGELES, CALIF.

THE California Heart Association several years ago asked its members to pool their experiences in regard to untoward reactions from carotid sinus stimulation. Seven instances of hemiplegia which occurred immediately after carotid sinus stimulation were reported by members of the association. This communication, therefore, is submitted as a joint report.

Mechanical stimulation of the carotid sinus is now a common clinical diagnostic procedure and is accepted as a routine in complete neurological examinations. No serious untoward effects ordinarily occur. It is the purpose of this communication to describe these seven cases, to emphasize that this procedure is not always without danger, and to discuss the implications of the findings in relation to the mechanism of the carotid sinus reflex. In addition, several unusual, previously undescribed clinical manifestations of carotid sinus sensitivity are reported. One patient for years had had spontaneous, transient attacks of right-sided hemiplegia and dizziness. In this patient, right hemiplegia was reproduced by left carotid sinus stimulation. The preceding episodes of transient paralysis thus were a result, we believe, of spontaneous stimulation of the carotid sinus. Another patient suffered mental lapses, disorientation, and dizziness. These spontaneous attacks were duplicated by carotid sinus stimulation.

In September, 1941, Marmor and Sapirstein[1] reported the case of a patient who developed bilateral thrombosis of the anterior cerebral arteries following stimulation of a hypersensitive sinus. Levine[2] reported a single instance of hemiplegia after the procedure. The most complete study of hypersensitivity of the carotid sinus was done by Weiss and his collaborators.[3] The clinical manifestations described were dizziness and syncope with or without convulsions. No instances of transient or persistent hemiplegia were described.

Ten instances of untoward response are reported in this study. Of these ten cases, only seven presented sufficient evidence to be certain that the hemiplegia was a direct result of mechanical stimulation of the carotid sinus. It is possible that in two other cases hemiplegia occurred as a direct result of the stimulation of the carotid sinus, but, in one (Case 8), twenty-four hours elapsed after stimulation before hemiplegia appeared, and in another, not reported here, the data were not sufficient.

The following members of the California Heart Association contributed material for this report: Louis E. Martin, Harold H. Rosenblum, Myron Prinzmetal, E. Richmond Ware, Lewis T. Bullock, Ferrall H. Moore, Lester S. Lipsitch, William C. Boeck, Donald J. Frick, Morris H. Nathanson, and Edward C. Rosenow. Miss Marjorie Edwards, Executive Secretary, assisted in compiling the data.

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TABLE I. PATIENTS WITH HEMIPLEGIA FOLLOWING CAROTID SINUS STIMULATION

CASE	SEX	AGE (YRS.)	BLOOD PRESSURE	DIAGNOSIS	COMPLAINTS	TYPE OF RESPONSE	CAROTID SINUS, PRESSURE	POSITION OF PATIENT	HEMIPLEGIA, SIDE, ONSET, DURATION
1	M	60	No data	Arteriosclerosis (retinal)	Dizziness, faintness, no loss of consciousness	Asystole, 15 seconds, B.P. 100/68	Moderate on right	Sitting	Left hemiplegia; onset immediate; duration 6 weeks
2	M	60	160/65	Syphilitic aortitis with aortic regurgitation	Dizzy spells	No asystole but bradycardia Asystole, 5 seconds, bradycardia 15 seconds	Very light on right Heavy on right	Recumbent	Left hemiplegia; onset 15 minutes after; duration 1 hour Left hemiplegia; onset immediate; duration 5 minutes
3	M	55	195/115	Arteriosclerosis, hypertension (old infarct)	Angina pectoris (severe)	Asystole, loss of consciousness	Light on right	Recumbent	Left hemiplegia (75% loss of strength); onset immediate; duration 2 weeks plus
4	M	54	No data	Arteriosclerosis, hypertension	Dizziness	Bradycardia, no loss of consciousness, faintness	Light on right	Recumbent	Left upper extremity; onset immediate; duration 1 day
5	M	53	153/100	Arteriosclerosis	Transient right hemiplegia, dizziness	No bradycardia or drop in B.P.	Light on left	Recumbent	Right hemiplegia; onset immediate; duration 1 week plus
6	F	42	No data	No data	Dizziness, headaches	No details	Chiropractic massage on right	Sitting	Left hemiplegia; onset immediate; duration 2 weeks plus
7	M	60	160/110	Arteriosclerosis	Syncopal attacks	Loss of consciousness	Moderate (side unknown)	Recumbent Sitting	Onset immediate; duration several months; complete recovery

CASE 1.—A white man, aged 60 years, a laborer, was admitted to the Los Angeles County General Hospital, complaining of dizziness and frequent attacks of faintness without loss of consciousness. These symptoms were precipitated by moving the head quickly from side to side, or by suddenly sitting up. He had experienced severe nausea but no vomiting or complete loss of consciousness. The physical examination showed a well-nourished and well-developed, florid man of sthenic habitus. No unusual sclerosis of the large arteries was noticed. The retinal arteries showed slight tortuosity and venous compression. Moderate pressure on the right carotid sinus was performed while the patient was sitting. This was not believed to be sufficient to obliterate the artery completely. The following note describes the succeeding events: Within approximately forty-five seconds the patient complained of dizziness. The pressure immediately was released. Ventricular standstill was noted for about fifteen seconds. He did not become unconscious at any time. Examination immediately afterward revealed the following significant findings: The patient was confused. There was left facial palsy. The left pupil was slightly larger than the right. Slight deviation of the tongue to the left was noted. There was flaccidity and weakness of the left arm and leg. The reflexes of the left upper extremity were absent. The left patellar reflex was hyperactive and the patient had a left positive Babinski reflex. Improvement in mentality began five days later when he was more alert, and on the next day some movement was noted in the left leg. Two weeks later some motor function was present in the left hand. He was generally stronger with increasing use of the left leg. Five weeks later he was walking about the ward, and on discharge, six weeks after the onset, there was only slight remaining weakness in the left arm and leg.

CASE 2.—A 60-year-old man, treated at the outpatient department of the Lane Hospital of the Stanford University School of Medicine in San Francisco, had syphilitic aortitis with aortic insufficiency and mild hypertension. He began to have dizzy spells while shaving. Right carotid sinus pressure produced some slowing of the heart with definite reproduction of the dizziness. Ten to fifteen minutes after carotid sinus stimulation, the patient was unable to walk and could not move the left arm or leg. There was no total paralysis. He was sent to the San Francisco City Hospital, where pressure on the right carotid sinus again caused temporary paralysis. After each stimulation the patient became numb and paralyzed on the left side. The paralysis disappeared after about fifteen minutes. There was a period of asystole for five seconds, followed by mild bradycardia for fifteen seconds.

CASE 3.—A 55-year-old man showed arteriosclerotic heart disease and angina pectoris following a probable myocardial infarction occurring two years previously. The right carotid sinus was massaged lightly while the patient was in the upright position. This was followed immediately by cardiac standstill and loss of consciousness for a few minutes. Slow recovery of consciousness occurred during the following fifteen to twenty minutes, at which time it was found that there was a weakness of the left hand and left leg, estimated at approximately 25 per cent of the strength of the opposite member. Recovery from the weakness of the left side was only partial when he was last seen approximately two weeks after the episode.

CASE 4.—The detailed findings of this case are not available, but hemiplegia occurred also in a man with hypertension and arteriosclerosis. Light pressure was applied over the right carotid sinus producing marked cardiac slowing followed by faintness, without loss of consciousness. Immediately afterward, marked weakness of the left upper extremity was observed. This disappeared the following day.

CASE 5.—A 53-year-old man complained of attacks of dizziness and syncope. The episodes were associated with double vision and impairment of coordination. On several occasions the right arm became weak and numb during the attacks. Frequently he was unable to talk during a seizure. The attacks were of abrupt onset. One morning he could not brush his teeth because of weakness and clumsiness of the right hand. The function of the right arm was gradually restored during the ensuing thirty minutes. These episodes had occurred frequently, and sometimes several times daily, from 1937 until he was first seen in 1941. They usually lasted about five minutes. After neurological examination it was thought that the patient had a psychoneurosis with transient hysterical paralysis of the right arm.

The blood pressure was 156/90. The attacks occurred occasionally on turning the head from one side to the other. The left carotid sinus was very lightly massaged. The stimulation was hardly begun when the patient stated that he felt dizzy and unsteady. There was no change in the heart rate. His face became congested, the eyes rolled, and the breathing was stertorous. He was laid immediately on the table, and his right arm fell limp to the side. There was complete paralysis of the right side. He was somewhat confused mentally but answered questions intelligently. There was no significant change in the blood pressure. After the administration of amyl nitrite, he felt better. After two hours the right leg recovered, but the right arm remained limp and helpless. Three and one-half hours later he was able to raise the right arm but could not flex the fingers. Neurological examination four days later revealed some weakness of the right eyelid and the muscles of the right forearm, and some weakness of the right angle of the mouth. The closing mechanism of the right eyelid appeared impaired. There was some weakness of the external and internal hamstrings of the right thigh. The right biceps, triceps, and supinator reflexes were slightly exaggerated, whereas those on the left were normal. The right patellar reflex was exaggerated. An intermittent positive Babinski sign was occasionally noted on the right. The patient was observed for several months following this stimulation, and he continued to have frequent attacks of the same character.

CASE 6.—A white woman, aged 42 years, developed a very severe headache on the top of the head following a cold. It was made worse by bending the neck. She had five chiropractic treatments for this headache. She stated that, during the last treatment, the chiropractor pressed rather firmly on the right side of her neck below the angle of the jaw, and immediately she became dizzy and faint but not unconscious, and then discovered that she could not move her left arm or left leg. Her husband entered the office and found her speaking incoherently and unable to walk. He had to carry her to the car. The left side of the face, the left arm, and the left leg were paralyzed, and she complained of numbness over the left side of the body. She was removed later to the Los Angeles Good Samaritan Hospital. There was no past history of symptoms referable to the cardiovascular system. The blood pressure measured 140/90. The neurological examination revealed the pupils to be equal, regular, and reacting to light and accomodation. There was a horizontal nystagmus when she looked in either direction. The movements of the left eye were slower than those of the right, but apparently there was no complete paralysis of any of the extraocular muscles. There was weakness of the left side of the face with hypertonicity on the right. The speech was thick at times, but there was no dysphagia or aphasia. There was only slight movement of the group of shoulder muscles on the left side, with almost complete paralysis of the left upper extremity. This arm was spastic with markedly exaggerated reflexes and pseudoclonus. Sensation was present on the left side but was slightly less than on the right. The knee could be lifted slightly on effort. There were exaggerated reflexes and pseudoclonus. There was a suggestive Babinski reaction on the left. The neurologist's impression was that "the history and findings are suggestive of cerebral thrombosis, secondary to manipulative procedures. An electroencephalogram might yield some information."

CASE 7.—A man, 60 years of age, had generalized arteriosclerosis and had had a very hypersensitive carotid sinus reflex with many rather severe syncopal attacks which could be induced by moderate pressure on either the right or left carotid sinus. The blood pressure was 160/110. Immediately following one induced attack, the patient developed a complete hemiplegia. He made a complete recovery from his hemiplegia although the symptoms lasted for several months. His syncopal attacks have been controlled fairly well by quite large doses of phenobarbital.

In the following case the hemiplegia cannot be ascribed definitely to carotid sinus pressure inasmuch as it occurred the day following the stimulation.

CASE 8.—A man, 72 years of age, complained of dizzy spells of several years' duration. He had moderate hypertension: his blood pressure was 170/100. There was no definite cardiac enlargement. General physical examination showed nothing abnormal. Pressure on

the right carotid sinus, made in the supine position, resulted in marked dizziness and cardiac arrest of several seconds' duration. When the patient assumed the erect position, he seemed very unsteady and complained of severe dizziness. He lay down for a short period but on leaving the office was still unsteady. The examination was performed in the morning, and the patient remained at home in the afternoon. He was still conscious of lessening degrees of dizziness. He slept well, and the following morning on awakening he found that he was unable to move his left arm and left lower extremity. The muscular weakness improved quite rapidly so that within two weeks he was able to be up and around. He was followed for about a year after this episode with no significant change in the clinical course.

OTHER CEREBRAL DISTURBANCES

Distressing cerebral complications, besides hemiplegia, have been reported several times. Weiss[3] stated that he had observed but one patient with untoward symptoms. For several days following a spontaneous attack, one of his patients felt weak and exhausted. Moderate pressure on the sinus of this patient produced weakness, dizziness, and partial syncope in three to five seconds, and for several days thereafter she did not feel well. Two instances of cerebral irritability were reported in our series.

CASE 9.—A man, aged about 65 years, had arteriosclerosis and early senile dementia with mental lapses, disorientation, and dizziness. Pressure was made on the right carotid sinus. Asystole lasting about five seconds was produced. Following this he became very pale and was silent during the remainder of the office visit. His brother called the next day and stated that, following the pressure on the carotid sinus, his mental condition was much impaired for about twenty-four hours. He had remembered nothing and was completely disoriented.

CASE 10.—A robust Russian man, aged about 55 years, complained of dizzy spells. He gave a very clear history and seemed very rational. Pressure was applied on the right carotid sinus twice, once with the patient recumbent, and once with the patient upright. He acted peculiarly during the remainder of the examination. Following the examination, he was very excitable and extremely irrational. He drove his niece, a nurse, home. She stated that he was unable to drive safely and that they narrowly escaped several accidents. He acted very queerly at home, this condition lasting about thirty-six hours. He made a complete recovery but stated that the pressure on his neck made him feel "crazy." There was only slight bradycardia produced by pressing his sinus.

DISCUSSION

From an analysis of the first seven cases it is apparent that mechanical stimulation of the carotid sinus is not as innocuous as generally is believed, and it may be followed by more or less serious paralysis. The great majority of the patients were elderly and had arteriosclerosis and hypertension. The patients described by Marmor and Sapirstein[1] and by Levine[2] were also arteriosclerotic. It would appear, therefore, that, although stimulation of the carotid sinus may be harmless in young people, the procedure should be utilized with caution in elderly persons with arteriosclerosis.

The mechanism by which the paralysis occurs is worthy of comment. In six instances the right carotid sinus was stimulated and the paralysis was on the left side. In one instance, the left carotid sinus was massaged and the paralysis was on the right side. Thus it is clear that the paralysis is contralateral and the cerebral effect must be ipsolateral to the side of carotid sinus stimulation. It has been shown by Weiss[3] that the cerebral ischemia following

pressure is not mechanical due to occlusion of the carotid artery. Furthermore, the hemiplegia in one patient (Case 5) abruptly followed light massage with very little pressure over the artery and with no change in the heart rate or blood pressure. The cerebral effect apparently is due to a direct unilateral cerebral action. Recent work by Engel and his co-workers[4] offers additional evidence for this concept. They observed abnormalities of the electroencephalogram on the same side as the carotid sinus pressure in a patient with a direct cerebral reflex type of hypersensitive carotid sinus, that is, with no fall in blood pressure and no bradycardia. Interestingly, there occurred clonic spasms of the right arm and leg when the left cortex was affected by left carotid sinus pressure, and the left side reacted when the right carotid sinus was stimulated. Whether the abnormal cerebral waves are secondary to reflex vasoconstriction or are due to a direct cortical effect, is unknown. The usual concept of hemiplegia would suggest that the fundamental cerebral disturbance in our patients was due to ischemia brought about by reflex vasoconstriction of the ipsolateral side. A direct unilateral cerebral effect from carotid sinus pressure, therefore, would appear to be more important in our patients than the production of cardio-inhibition or vasodepression, inasmuch as the cerebral effect producing the paralysis always was localized on the side of the pressure. This is corroborated by the work of Galdston and his collaborators.[5] They found that syncope and convulsions in certain patients would result from stimulation of the side that produced little or no bradycardia or drop in blood pressure, but that stimulation of the side which caused marked circulatory response would not produce these symptoms.

That the cerebral effect following carotid sinus pressure is not equally distributed bilaterally, but is predominantly ipsolateral, is suggested by many of the cases reported by Weiss.[3] The initial convulsive twitchings, numbness, and tingling were always contralateral. In describing the patients whose symptoms arose presumably from a direct cerebral reflex, he said, "Depending on the degree and duration of pressure, the symptoms consisted of faintness and pallor of the face followed by unconsciousness, and, in most cases by convulsive twitchings which usually began on the contra-lateral side and became generalized. . . . Numbness and tingling of the extremities were prominent symptoms usually starting in the contra-lateral extremities and spreading to the whole body before actual fainting occurred." Even in Weiss' cases where syncope was produced by cardio-inhibition or a drop in blood pressure, there was often evidence of a predominating ipsolateral cerebral effect. The induction of such symptoms and signs as contralateral numbness, tingling, and convulsions of the extremities and ipsolateral numbness of the face, suggests a direct unilateral cerebral reflex mechanism, particularly since prolonged occlusion of the carotid artery below the sinus failed to induce any such symptoms. It is interesting, in view of the findings in our cases, that in none of his patients did the findings progress to hemiplegia.

It would appear that in many of the persons of the type described in this report there is advanced cerebral arteriosclerosis with great impairment of the blood supply to the brain. Whereas a temporary disturbance of the blood supply to a normal brain from carotid sinus stimulation would seem innocuous,

any further reduction of the blood flow in the brain with an already impaired blood supply may produce deleterious effects. This could explain the transient hemiplegia lasting only a few minutes. However, in the patients with more persistent hemiplegia following carotid sinus stimulation, a more permanent mechanism, either thrombosis or a small hemorrhage, would seem responsible. Thrombosis of the anterior cerebral arteries was observed by Marmor and Sapirstein.[1] In previous reports on carotid sinus sensitivity the predominant clinical manifestation described was dizziness and syncope, with or without convulsions. Stern[6] described one case with gastrointestinal manifestations. Friedman[7] reported two instances with anginal syndrome. In the present report are described two instances in which the patients had bizarre, previously undescribed manifestations, apparently due to spontaneous carotid sinus stimulation because they could be reproduced by carotid sinus pressure. One patient (Case 5), in addition to the dizziness and the other usual manifestations of carotid sinus sensitivity, had varying degrees of weakness of the right arm which was reproduced by carotid sinus stimulation. In another patient with marked cerebral arteriosclerosis and frequent episodes of loss of memory and disorientation (Case 9) stimulation of the carotid sinus produced a very severe attack lasting twenty-four hours. Thus, the additional cerebral ischemia induced by carotid sinus stimulation produced paralysis in the first patient, while, in the second patient, it enhanced the mental disturbances due to the cerebral ischemia of senility.

SUMMARY AND CONCLUSIONS

1. Seven instances of contralateral hemiplegia following carotid sinus pressure are reported.

2. Transient hemiplegia as a manifestation of hypersensitive carotid sinus activity is suggested by its reproduction in a patient who had had attacks for years.

3. Two patients were observed with mental aberration following carotid sinus pressure.

4. Carotid sinus pressure in the middle-aged or elderly arteriosclerotic patient may be productive of untoward results and should be applied cautiously.

REFERENCES

1. Marmor, J., and Sapirstein, M. R.: Bilateral Thrombosis of Anterior Cerebral Artery Following Stimulation of a Hypersensitive Carotid Sinus, J. A. M. A. **117**: 1089, 1941.
2. Levine, S. A.: Clinical Heart Disease, Philadelphia, 1945, W. B. Saunders & Co., p. 317.
3a. Weiss, S. O., and Baker, J. P.: The Carotid Sinus Reflex in Heart Disease. Its Role in the Causation of Fainting and Convulsions, Medicine **12**: 297, 1933.
b. Weiss, S. O., Capps, R. B., Ferris, E. B., and Munro, D.: Syncope and Convulsions Due to a Hyperactive Carotid Sinus Reflex, Arch. Int. Med. **58**: 407, 1936.
4. Engel, G. L., Romano, J., and McLin, T. R.: Vasodepressor and Carotid Sinus Syncope. Clinical, Electroencephalographic and Electrocardiographic Observations, Arch. Int. Med. **74**: 100, 1944.
5. Galdston, M., Goldstein, R., and Steele, J. Murray: Studies of the Variation in Circulatory and Respiratory Responses to Carotid Sinus Stimulation in Man, AM. HEART J. **26**: 213, 1943.
6. Stern, J. E.: Abdominal Manifestations of the Hyperactive Carotid Sinus Reflex, J. A. M. A. **110**: 1986, 1938.
7. Friedman, M.: The Anginal Syndrome as a Manifestation of Hyperactivity of the Carotid Sinus, AM. HEART J. **29**: 37, 1945.

TRANSITORY A-V BLOCK OCCURRING DURING SCARLET FEVER

W. D. Paul, M.D.,* and C. Rhomberg, M.D.,* Iowa City, Iowa,
and Julia Cole, M.D., Ames, Iowa

THAT the heart may be involved in scarlet fever had been recognized for many years. Many reports and opinions have been recorded regarding the nature of the myocarditis occurring during the acute phase of this disease and the chronic valvular disorders which follow. Rosenbaum[1] reported 1,770 cases of scarlet fever, in 106 of which there were definite cardiac complications. A diagnosis of myocarditis was made in 88 of these cases, and was based upon clinical observations such as changes in heart rate, variation in the size of the heart, disturbances of conduction, et cetera. Swift,[2] in a treatise on the heart in infection, stated that cardiac complications occurred infrequently in scarlet fever, and he classified them as (1) toxic, (2) allergic, and (3) septicopyemic. The last two involve valvular damage. The "toxic" manifestations, which are regarded as similar to those in diphtheria, are characterized by signs of cardiac weakness and are often accompanied by bradycardia. No mention of electrocardiographic changes was made.

Shookhoff and Taran[3] reported 50 cases of scarlet fever in which electrocardiographic studies were made. Bradycardia was found in 25 per cent, but no lengthening of the P-R interval or other disturbances of conduction was observed. Place[4] concluded that myocarditis in scarlet fever is very rare; he stated that since the use of the electrocardiogram "no well marked case (of myocarditis) has occurred in our wards in several thousand cases." Collaborating with Faulkner and Ohler, Place[5] reported 171 cases in which electrocardiographic studies were made. Abnormal tracings were secured in 11, or 6 per cent. In five of the 11 the abnormality consisted merely of prolongation of the P-R interval beyond 0.2 second, and in six there were T-wave changes. The majority of these changes developed between the eighteenth and thirty-fourth days, and the degree of electrocardiographic abnormality was not influenced by the severity of the illness. Wickstrom[6] observed prolongation of A-V conduction time beyond 0.2 second in five of a group of 100 patients. Schwarz[7] studied 65 patients with scarlet fever clinically and electrocardiographically, and observed no electrocardiographic evidence of cardiac involvement. Berger and Olloz[8] reported finding electrocardiographic evidence of myocarditis in four of a series of 66 cases, but mentioned no instance of complete heart block. Holz[9] reported seven cases of scarlet fever, complicated by joint involvement, in which electrocardiographic evidence of conduction disturbance was found. In all of these cases the P-R interval was prolonged, and, in one case, partial block, with Wenckebach periods, was observed. Beer[10] found electrocardiographic evidence

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*From the Department of Internal Medicine, State University of Iowa, Iowa City.

of conduction disturbance in 14 cases of scarlet fever with joint involvement. Electrocardiographic abnormalities consisted of prolongation of the P-R interval or partial heart block. Roger[11] cited the case of a 21-year-old man whose heart rate dropped to 52 and stayed there for three days. He concluded that the focus of irritation was bulbar, because, under the influence of small doses of atropine, the heart rate rose to 64. Bernstein[12] reported the case of an 18-year-old boy who developed A-V dissociation after scarlet fever. Electrocardiographic studies were not made during the attack of scarlet fever, but a transient bradycardia was observed on the eighteenth day of the illness. Subsequently, this patient developed attacks of dizziness, blurred vision, dyspnea, and brief periods of unconsciousness. When he was re-examined about fourteen or fifteen months later, complete heart block and cardiac decompensation were observed.

Although no attempt was made to cover the literature, no mention of complete heart block occurring during scarlet fever was found. For this reason, and because of the difference of opinion regarding the nature of the myocardial involvement in this disease, two cases of complete heart block occurring during the course of scarlet fever are reported. Both were observed on the Medical Isolation service of the State University of Iowa Hospital in 1936.

CASE 1.—P. H. was born in 1918, and was considered a healthy infant. He had the usual diseases of childhood, but no scarlet fever, diphtheria, rheumatic fever, chorea, or frequent tonsillitis. There was no history of shortness of breath, heart consciousness, precordial pain, or syncope. About four days prior to admission to the hospital he complained of a slight head cold, general malaise, and fever. On the third day of his illness he noticed sore throat and hoarseness, and on the day of admission, flushing of the face and a diffuse rash over the chest.

Physical Examination.—The patient was a well-developed, well-nourished white man, 18 years of age. There was a punctate, erythematous rash which blanched on pressure and was most marked in the axillae and over the abdomen and thighs. The hearing and vision were normal. Ophthalmoscopic examination was negative. The teeth were in good condition. The tongue was coated on the dorsum and clear at the edges, where the papillae were prominent. The pharynx was very red, the pillars were edematous, and the tonsils were slightly enlarged. Small pin-point macules were present over the soft and hard palate. The lungs were normal to auscultation and percussion. The heart was of normal size, the rhythm was normal, and the sounds were of good quality. No murmurs were heard. The pulmonic second sound was slightly accentuated. The arterial blood pressure was 124/70. The abdomen, rectum, and extremities were normal. There were no abnormal neurological signs.

Laboratory Data.—The initial blood cell count showed 4,096,000 erythrocytes and 8,800 leucocytes, of which 78 per cent were polymorphonuclears, 17 per cent were lymphocytes, and 5 per cent were endothelial cells. The hemoglobin was 90 per cent (Sahli). The blood Wassermann reaction was negative. The urine was entirely normal on repeated examination. Throat cultures were negative for *Corynebacterium diphtheriae,* but positive for *Streptococcus hemolyticus.* The Dick test was negative, and the Schultz-Charlton reaction revealed a blanching of the rash over an area of 4 centimeters.

Subsequent Course.—At the time of admission the patient's temperature was 100° F., his heart rate was 86, and his respiratory rate was 18. He was given routine treatment, consisting of rest in bed, a high fluid intake, and a soft diet. No antitoxin was administered. His temperature was normal at the end of forty-eight hours and his angina was subsiding. The rash disappeared and desquamation started. He continued to be hoarse, and examination of the pharynx revealed chronic laryngitis with an acute exacerbation of the angina.

On the tenth and eleventh hospital days the temperature rose to 103° F. The only new observation at this time was tenderness of a cervical lymph node which subsided with local application of ice. On the fourteenth hospital day the temperature rose to 101.8° F. and, for the next ten days, fluctuated between normal and 103.6° F. The laryngitis became more severe. Blood cultures taken during this period showed no growth. The heart rate at first increased slightly with the rise in temperature. However, on January 31, the fifteenth hospital day and the nineteenth day of illness, the heart rate suddenly dropped to 40. Examination showed that the left border of the heart was a little outside the midclavicular line.

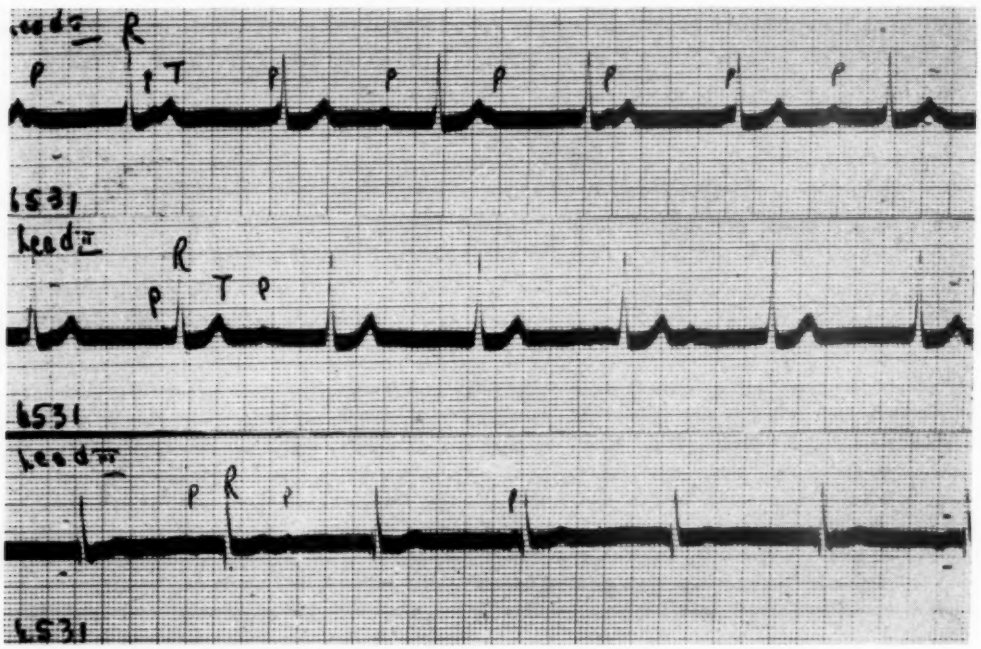

Fig. 1.—Case 1. P. H.: Electrocardiogram taken on the 15th hospital day, Jan. 31, 1936. This shows complete A-V block, the auricular rate being 80, the ventricular rate 56.

A systolic murmur was heard at the apex. The rhythm was regular except for an occasional pause; the pulmonic second sound was loud and rather snappy. The arterial blood pressure was 135/70. An electrocardiogram taken on this day showed complete heart block, with an auricular rate of 80, and a ventricular rate of 56, per minute. There was no associated dyspnea or heart consciousness. On the next day the same cardiac abnormalities were observed. On February 4 the cardiac rate was 80 per minute, and electrocardiographic study showed normal mechanism, with a P-R interval of 0.19 second, an inverted P_3, a large T_1 and T_2, and an isoelectric T_3. During the next week the cardiac rate varied between 60 and 90 per minute, but repeated electrocardiograms showed a normal mechanism. On February 6, the twenty-first hospital day and the twenty-fifth day of his illness, the patient developed pain in the shoulders and knees, without redness, swelling, or heat. He also had acute abdominal pain and a leucocytosis of 23,000. On the twenty-fourth hospital day the joint pain, abdominal pain, and laryngitis subsided; the temperature returned to normal and remained there. Daily examination of the urine for blood and albumin failed to reveal their presence. At the time the patient was discharged, on the forty-fifth hospital day, after almost three weeks of normal temperature, the heart rate was 70, the heart was of normal size, the systolic murmur had disappeared, and the pulmonic second sound was no longer loud and snappy. An electrocardiogram shortly before the time of discharge showed a P-R interval of 0.14 second.

The patient returned to the hospital June 23, 1936, for re-examination. After returning home he had remained in bed for one month, and, following this, had restricted his exercise. He had had no symptoms referrable to the nasopharynx or the cardiovascular system. His appetite had remained good and he had gained 10 pounds in weight. Throughout this time he had been afebrile and his heart rate had varied between 60 and 80 per minute. Physical examination was essentially negative. The heart was of normal size, the rhythm was normal, no murmurs were heard, and the pulmonic second sound was somewhat accentuated. The arterial blood pressure was 160/100. The urine was normal. An electrocardiogram showed normal mechanism; the P-R interval was normal, and there was no abnormal deviation of the electrical axis. This patient returned for re-examination regularly throughout the next two years. At no time did the history indicate cardiac involvement; examination of the heart was negative and electrocardiographic studies were normal. He has been in the Army for the past three years and is now a captain in the Air Corps on active combat duty in the Southwest Pacific area.

CASE 2.—R. G., according to his history, gave no evidence of any cardiac involvement prior to Jan. 15, 1936, when he was admitted to the hospital during an attack of scarlet fever. He was born in 1916 and had been considered a healthy infant. He had had the usual diseases of childhood, but no scarlet fever, diphtheria, rheumatic fever, chorea, or frequent tonsillitis. There was no history of heart consciousness, precordial pain, shortness of breath, or syncope. In 1926 he developed gonorrheal ophthalmitis on the right and secondary glaucoma. Two days before admission he noticed a slight sore throat and some fatigue. The following day his throat was quite painful and he had a rash over his abdomen. He was admitted on the third day of his illness.

Physical Examination.—The patient was a well-developed, well-nourished white man, aged 20 years. There was a diffuse, punctate rash which was most prominent over the chest and abdomen. Hearing was unimpaired, but there were loss of vision and corneal opacity on the right. The teeth were normal. The tongue was coated with a grayish exudate, and the papillae at the margins were hypertrophied. The oropharynx was red, and there were pinpoint macules over the soft and hard palates. A few cervical lymph nodes were palpable. The thyroid was not enlarged. Examination of the chest was negative. The heart was normal in size, the rhythm was regular, and no murmurs were heard. The arterial blood pressure was 130/80. The adomen, rectum, and extremities were essentially normal. No abnormal neurological signs were elicited.

Laboratory Data.—At the time of admission the blood cell count showed 4,650,000 erythrocytes and 20,200 leucocytes, of which 87 per cent were polymorphonuclears and 13 per cent lymphocytes. The hemoglobin was 90 per cent (Sahli). Repeated urine examinations were negative. The blood Wassermann reaction was negative. Throat cultures were negative for *Corynebacterium diphtheriae,* but positive for *Streptococcus hemolyticus.* The Dick test was negative. The Schultz-Charlton reaction showed a large area of selective blanching.

Subsequent Course.—On admission this patient had a temperature of 101° F., a heart rate of 110, and a respiratory rate of 23 per minute. His temperature fluctuated between normal and 100° F. for the following eleven days, and then became normal. Treatment was mainly symptomatic and supportive, and consisted of rest in bed, a high fluid intake, and a soft diet. Antitoxin was not given. Throughout this time the patient was without complaint and in good spirits; the angina cleared up, the rash disappeared, and desquamation began. On the morning of the eighteenth hospital day and the twenty-first day of illness, there was an unexplained rise in temperature to 101.4° F. On January 31, the nineteenth hospital day, the patient suddenly complained of marked weakness. The pulse rate was recorded by the nurse as 38 per minute. He was examined shortly after the onset of the weakness and was found to be pale and perspiring profusely. He complained of some nausea and weakness, but there was no heart consciousness, cardiac pain, dyspnea, or cyanosis. The patient stated that he felt as if he were "floating away." The cardiac and radial pulse rates were 26, and the rhythm was slightly irregular. The heart was normal in size, the sounds were of good quality, and no murmurs were heard. Electrocardiographic study on the same day showed

complete A-V dissociation, with an auricular rate of 107 and a ventricular rate of 25 per minute, and with ventricular standstill up to five seconds.

The patient continued to complain of some weakness and nausea during the following forty-eight hours, but developed no other complaints. He was afebrile during the remainder of his hospital stay except for rises of temperature to 99.8° F. on the twenty-first and twenty-second hospital days. Electrocardiographic studies were made once or twice a day. On February 1, the twentieth hospital day, partial A-V heart block was present. This persisted until February 4, when simple prolongation of the P-R interval with dropped beats was observed. The P-R interval varied between 0.32 and 0.41 second. This type of curve was obtained until February 11, the thirtieth hospital day, when normal mechanism, with a P-R interval of 0.16 and ventricular rate of 62, was present. The T waves, which had been biphasic, were now upright in all leads. From this time until the day of discharge, Feb. 21, 1936, the electrocardiograms were normal.

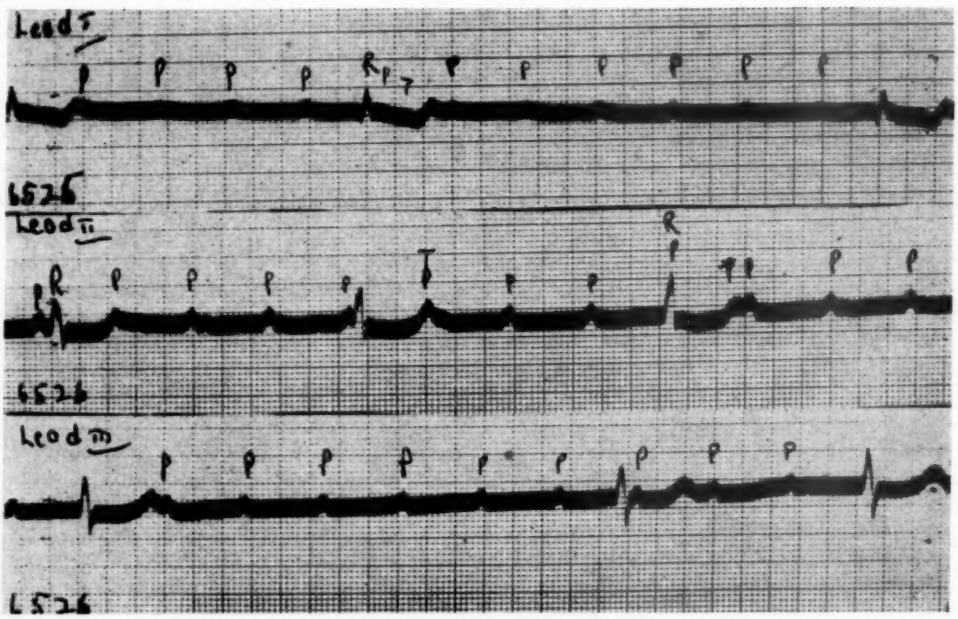

Fig. 2.—Case 2. R. G.: Electrocardiogram taken on the 19th hospital day, Jan. 31, 1936. The auricular rate was 107; the ventricular rate was 25. Note long periods of ventricular asystole.

The patient returned for re-examination June 17, 1936. For one month after discharge from the hospital he had remained in bed, and for the following three months he had been on very restricted exercise. He had had no nasopharyngeal or cardiovascular symptoms. His temperature had been observed daily and had been normal throughout the entire period. His heart rate had varied between 70 and 96 per minute. He had gained 20 pounds. Physical examination was entirely negative. The heart was of normal size, and the rhythm regular. No murmurs were heard. The arterial blood pressure was 110/82. The urine was normal. The electrocardiogram was normal.

This patient has been examined repeatedly throughout the past nine years. He was last seen on April 26, 1945, at which time the history was essentially negative; physical examination was negative except for the glass eye on the right. The loss of this eye alone has blocked his induction into the Army on six occasions. He has passed examinations for life insurance, works as a chiropodist, and has had but four weeks' vacation during the past nine years. The electrocardiogram, including Lead IV F, was entirely normal. The three standard leads could be superimposed on the curve taken at the time he left the hospital in February, 1936.

Because the manifestations of the acute and late phases of cardiac involvement in scarlet fever are analogous to those of rheumatic fever, many authorities have postulated that the cardiac complications which occur during the acute stage or following upon scarlet fever indicate part of a rheumatic cycle. Conduction disturbances are considered to be relatively common during acute rheumatic fever, and have occurred during other acute infectious diseases. Rosenberg[13] recently reported two cases of epidemic parotitis accompanied by temporary electrocardiographic evidence of complete heart block. In most of these cases the disturbance in conduction proved to be transitory, and, as far as was ascertained, no evidence of residual cardiac involvement could be found. Unfortunately, these patients were not observed for any length of time after the initial illness.

Many investigators have described microscopic focal myocardial lesions in scarlet fever resembling those found in rheumatic fever. Fahr[14, 15] examined one series of nine and another of eleven postscarlatinal hearts. Small collections of round cells were common, but he believed he could differentiate them from Aschoff nodules. Schmorl (cited by Fahr[14]) described myocardial "rheumatic nodules" in a child who died of scarlet fever and had no previous history of rheumatism. Gross and Ehrlich[16] point out that the true Aschoff nodule does not attain its specific characteristics until after six weeks or more.

Although such lesions may be responsible for the chronic endocarditis and myocarditis which follow scarlet fever, they cannot be offered as a satisfactory explanation for the transitory cardiac murmurs and conduction disturbances which appear during the acute or early convalescent stages of the disease. These latter changes have been considered as manifestations of actual, although temporary, myocardial damage of the so-called toxic type.

Krauss[17] reported two cases of sudden death on the sixth and seventh days, respectively, of scarlet fever. At autopsy the heart was dilated and flabby, and infiltrations of round cells were present. Similar cases have been observed by Goldschmidt[18] and Gouget and Dechaux.[19] The latter authors cited over fourteen cases of sudden death occurring at various stages of the disease. They concluded that there is usually no pathologic change which would account for death, and suggested that the deaths occurring at the beginning of the disease resulted from massive intoxication of the whole central nervous system, whereas those which followed the usual course of the disease could be accounted for by the theory that "the condition of the nerve cells had been modified in some obscure way by the action of toxins, so that even a slight incidental cause, by producing in their neighborhood some abnormal stimulus, suffices to produce sudden or rapid death." The possibility of myocarditis or suprarenal lesions were also considered, but no mention of suprarenal lesions, especially hemorrhage, in scarlet fever could be found.

Weill and Mouriquand[20] reported a case of sudden death on the thirteenth day after onset of scarlet fever. At necropsy a soft, yellow-red, but otherwise normal, heart was found. Microscopic study revealed perivascular and interstitial round cell infiltration and fragmentation of the muscle fibers. These observations agree with those cited by earlier workers. Virchow[21] observed eight

hearts after death from scarlet fever, and found only a beginning fatty infiltration. In 1882, Litten[22] described the heart in the early stages as flabby and anemic, and, in cases of longer duration, as yellowish, with loss of cross-striations and the presence of fat droplets. Ott[23] reported the following post-mortem observations in the case of a 7-year-old boy who died of scarlet fever nephritis: the left ventricle was much enlarged, the muscle fibers were unchanged, there was a slight amount of round cell infiltration in the interstitial tissue, and the ganglion cells showed fine, granular degeneration of the protoplasm, solution of the nucleus, and pericellular edema. Romberg,[24] in 1891, examined the hearts of ten persons who died of scarlet fever, found parenchymal degeneration of muscle fibers and interstitial round cell infiltration, and stated that the heart ganglia were not remarkable. Aschoff,[25] in 1906, described five cases, in one of which there was infiltration of plasma cells subendocardially; in the others no parenchymal degeneration was found. The heart nerve centers were not examined. Selinoff,[26] in 1913, found that the pathologic changes in the ganglion cells were more marked than those in the heart muscle in a series of twelve cases. He stated that the myocardium suffers chiefly parenchymal degeneration, whereas one finds collapse of the Nissl bodies, vacuolar degeneration, and necrotic changes in the nerve cells.

Stegemann,[27] in 1914, examined 49 patients with scarlet fever, who ranged in age from 6 months to 12 years, in special reference to the heart ganglia. He divided these cases into three groups, depending upon the day of illness on which death occurred. Eighteen died before the fifth day. In these "severely toxic cases of short duration," the parenchymatous changes in the myocardium were not marked. With the "infectious form of long duration," acute parenchymous degeneration, fatty infiltration, and necrosis were seen. Interstitial round cell infiltration of the heart wall was absent in the former but present in the latter. Round cell infiltration in the stroma of the ganglia, fatty infiltration, and necrosis of the nerve cells, more marked in the severely toxic cases, were found as early as the first day. In all of the cases there were definite changes in the cardiac ganglia in the form of cellular accumulation in the stroma of the ganglion cells. Recently the existence of a conduction system in the heart has been questioned.[28] Nonidez[29] has demonstrated definite sinoauricular and auriculoventricular nodes, and main, right, and left bundles in the *Rhesus* monkey and dog. He also showed that the nodes are supplied by axons of neurons of the intrinsic cardiac ganglia.

In marked contrast to rheumatic fever and diphtheria, serious cardiac complications in scarlet fever are uncommon, and their occurrence seems to be a matter of chance. In spite of this fact, many hypotheses as to the mechanism of their production have been postulated, and much evidence has been accumulated in support of the various theories. The two cases of heart block reported above appear to be similar to those seen during mumps by Rosenberg; all occurred fairly early during the illness, without other evidence of cardiac involvement, and were transitory; they were due, in all probability, to toxic changes. Edema or early round cell infiltration with impingement on the conduction system could cause a temporary, but complete, A-V dissociation. Coincidence will account for

the fact that these two patients, unrelated and coming from widely separated towns developed the only complete heart block during scarlet fever to be recorded in recent literature on the same day and in the same room, within a few hours of one another.

REFERENCES

1. Rosenbaum, H. A.: The Heart in Scarlet Fever, Arch. Int. Med. 26: 424, 1920.
2. Swift, H. F.: The Heart in Infection, AM. HEART J. 3: 629, 1928.
3. Shookhoff, C., and Taran, L. M.: Electrocardiographic Studies in Infectious Diseases, AM. HEART J. 6: 541, 1931.
4. Place, E. H.: The Heart in Diphtheria and Scarlet Fever, New England J. Med. 207: 864, 1932.
5. Faulkner, J. M., Place, E. H., and Ohler, W. R.: The Effect of Scarlet Fever Upon the Heart, Am. J. M. Sc. 189: 352, 1935.
6. Wickstrom, J.: An Electrocardiographic Study of the Heart in Scarlet Fever, Acta Paediat., Supp. 4, 14: 1, 1933.
7. Schwarz, W.: Contributo allo studio della compromissione del cuore nella scarlattina, con particolare riguardo al miocardio, Pediatria 42: 267, 1934.
8. Berger, W., and Olloz, M.: Elektrokardiographische Untersuchungen bei Scharlach und Diphtherie, Schweiz. med. Wchnschr. 64: 992, 1934.
9. Holz, B.: Scharlachrheumatoid und Herzstörungen, München. med. Wchnschr. 86: 90, 1939.
10. Beer, A.: Über Reizleitungsstörungen bei Scharlach, Arch. f. Kinderh. 125: 194, 1942.
11. Roger, H.: Quelques maladies Infectieuses, D'apres les observations recueillies a l'hôpital d'isolement de la port D'Ambervilliers, pendant l'année, 1900, Rev. de méd. 21: 369, 508, 595, 1901.
12. Bernstein, M.: Auriculoventricular Dissociation following Scarlet Fever, AM. HEART J. 16: 582, 1938.
13. Rosenberg, B. H.: Electrocardiographic Changes in Epidemic Parotitis (Mumps), Proc. Soc. Exper. Biol. & Med. 58: 9, 1945.
14. Fahr, T.: Beiträge zur Frage der Herz- und Gelenkveränderungen bei Geleckrheumatismus und Scharlach, Virchows Arch. f. path. Anat. 232: 134, 1921.
15. Fahr, T.: Vergleichende Herzuntersuchungen bei Scharlach, Streptokokkeninfektion und rheumatischer Granulomatose, Beitr. z. path. anat. u. z. allg. path. 85: 445, 1930.
16. a. Gross, L., and Ehrlich, J. C.: Studies on the Myocardial Aschoff Body; Descriptive Classification of Lesions, Am. J. Path. 10: 467, 1934.
    b. Gross, L., and Ehrlich, J. C.: Studies on the Myocardial Aschoff Body; Life Cycle, Sites of Predilection and Relation to Clinical Course of Rheumatic Fever, Am. J. Path. 10: 489, 1934.
17. Krauss, T. F.: Sudden Death in Scarlet Fever, Report of Two Cases, J. A. M. A. 80: 454, 1923.
18. Goldschmidt, M.: Mort subite dans la Scarlatine, Bull. et mém. Soc. méd. d. hôp. de Paris 22: 521, 1905.
19. Gouget and Dechaux: On Cases of Unforeseen Death in Scarlet Fever, Internat. Clin. 3: 204, 1909.
20. Weill, E., and Mouriquand, G.: A propos de la mort imprévue par myocardite scarlatineuse, Presse Méd. 19: 643, 1911.
21. Virchow, R.: Quoted by Stegemann, A.[27]
22. Litten, M.: Beiträge zur Lehre von der Scarlatina, Charité-Ann., Berl. 7: 109, 1882.
23. Ott, A.: Beiträge zur Kenntniss der normalen und pathologischen Verhältnisse der Ganglien des menschlichen Herzens, Ztschr. f. Heilk. 9: 271, 1888.
24. Romberg, E.: Ueber die Erkrankungen der Herz muskel bei Typhus abdominalis, Scharlach und Diphtherie, Deutsches. Arch. f. klin. Med. 48: 369, 1891-1892.
25. Aschoff, L.: A Discussion on Some Aspects of Heart Block, Brit. M. J. 2: 1103, 1906.
26. Selinoff, A. Ye.: The Heart, Its Nerve Ganglia, and the Solar Plexus in Scarlatina, Russk. Vrach. 12: 629, 1913.
27. Stegemann, A.: Die pathologisch-anatomischen Veränderungen des Myocards und der Herzganglien beim Scharlach, Jahrb. f. Kinderh. 80: 491, 1914.
28. Glomset, D. J., and Glomset, A. T. A.: A Morphologic Study of the Cardiac Conduction System in Ungulates, Dog, and Man. I. Sinoatrial Node, AM. HEART J. 20: 389, 1940; II. The Purkinje System, ibid., 677.
29. Nonidez, José F.: The Structure and Innervation of the Conductive System of the Heart of the Dog and Rhesus Monkey, as Seen With a Silver Impregnation Technique, AM. HEART J. 26: 577, 1943.

THE RATE AND CONTROL OF THE BLOOD FLOW THROUGH THE SKIN OF THE LOWER EXTREMITIES

ROBERT H. GOETZ, M.D.
CAPE TOWN, SOUTH AFRICA

INTRODUCTION

MOST of our earlier published investigations concerning the control and rate of the blood flow through the skin were limited to the upper extremities.[20, 21, 23] Evidence presented by various authors,[11, 32, 37, 39, 45] however, goes to show that there are differences between the vasomotor responses of the vessels of the lower and upper extremities which, in man, as suggested by Pickering and Hess,[37] may be the result of the assumption of the upright posture. The vessels of the toes not only seem more susceptible to constrictor influences than those of the fingers,[39] but they are also relatively refractory to vasodilating agents.[5, 26]

This paper is, therefore, devoted to investigations of the rate and control of the blood flow through the skin of the toes. Apart from purely physiological considerations, accurate knowledge of the latter is essential both for diagnosis and evaluation of changes in the blood flow following therapeutic measures in peripheral vascular diseases. There occurs also a higher incidence of chronic occlusive arterial disease in the lower extremities than in the upper extremities which, in the light of the above data, may be of considerable significance.

The methods generally used for measuring tone and function of the blood vessels, like skin temperature and calorimetric readings, furnish either indirect indices of the blood flow only, or, as in the case of the oscillometric index, they do not deal with the peripheral circulation in a strict sense. For quantitative measurement of the blood flow, plethysmography has to be resorted to, and the number of different foot plethysmographs evolved during recent years[3, 12, 14, 28, 42, 50] indicates clearly the need for such methods. As pointed out in earlier papers, the results obtained with any limb plethysmograph necessarily refer to both the muscle and the skin enclosed within the instrument. Therefore, ambiguity will arise because the vessels supplying the skin do not respond necessarily in the same way to the same drug or stimulus as do the vessels supplying the muscle (often they react antagonistically[10, 16, 24, 31, 38, 40, 46]), nor need they be affected to the same degree by the pathologic process.

Also, even if the results obtained with limb plethysmographs were referable to skin only, their evaluation would be rendered difficult by the fact that, on account of anatomic differences in the arterial tree, the blood flow through the

From the Department of Surgery, University of Cape Town, South Africa.
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various skin areas enclosed cannot be expected to be uniform. Indeed investigations by various authors[1, 13, 23] demonstrate that "observations on the blood flow and vascular reactions in one skin area cannot necessarily be applied to others at the periphery."[13] Our optical finger plethysmograph was, therefore, adapted for investigations of the blood flow through the toes. The results obtained are not only strictly referable to the blood flow through the skin but they are also representative of the *ultimate* circulation, in contrast to the oscillometer, which deals with the *penultimate* circulation only.*

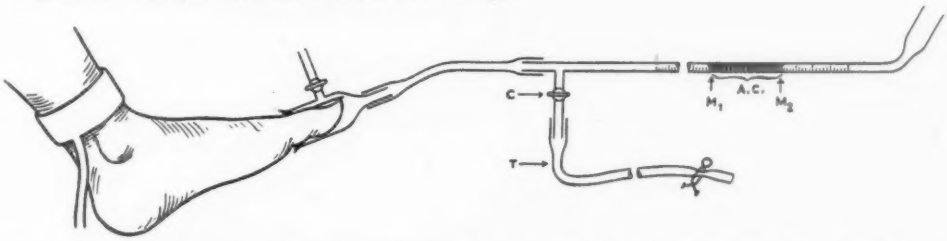

Fig. 1.—Toe plethysmograph as used for optical recording of the blood flow (for description see text).

METHODS AND MATERIAL

The methods used in this study follow closely those previously described,[21, 23] and for details the reader is referred to the preceding papers. Continuous volume records of the toes were obtained (Fig. 1) by enclosing a toe within a glass plethysmograph which was connected to a pipette graduated in 0.01 c.c. and containing a column of alcohol (A.C. in Fig. 1). When the plethysmograph was sealed with petrolatum and the taps were closed, the volume changes of the toes were transmitted to the alcohol column, the movements of which were enlarged and projected onto the paper of a recording camera, as previously described.[21] Registration was effected by the meniscus of the alcohol column (M_1 or M_2) which cast a shadow upon the photographic paper.[21] This arrangement is capable of exact and undistorted measurement of the changes in skin volume, differences of 0.001 c.c. being easily recorded. Whatever the enlargement, no calibration is required since the graduation of the pipette appears as white horizontal lines on the film, effecting automatic calibration of the system. Knowing that changes in respiration cause peripheral reflex constriction,[6, 19, 20] the respiratory movements were, as a rule, simultaneously recorded. In addition, the skin temperature of one or more toes next to the one measured plethysmographically was recorded simultaneously by means of thermocouples, and the pulsations of the dorsalis pedis arteries were registered by means of a Frank's capsule in many subjects (e.g., Figs. 6, *A*, and 23).

We have been using these methods since 1932 for both physiologic investigations and routine clinical tests, and the results communicated herein refer to tests carried out on more than two thousand subjects.

The observations were conducted in a draft-free and noiseless room and, unless otherwise stated, refer to "warm-handed" subjects who had normal cardiovascular systems. The room temperature was kept constant during the experiments. No effort was made to control the relative humidity, which has little effect on the dissipation of heat from the body at the room temperature used in this study.[39, 48] All the tests were performed after thirty to sixty minutes' rest. The subjects were, unless otherwise stated, resting comfortably in a type of Gatch bed, with the hips and knees flexed at about 60 degrees and the head and

*The terms *ultimate* circulation and *penultimate* circulation as used in this sense have been suggested by Professor C. F. M. Saint.

shoulders slightly elevated. Additional investigations were carried out with the legs elevated to about 45 degrees to study the effect of changes in posture upon the blood flow. Reflex dilatation of the vessels of the toes was obtained by immersion of one upper limb into water of 45° C. and covering the subject with blankets to prevent the dissipation of heat.

RESULTS

A. The Plethysmogram of the Toes During Rest.—The method is sensitive enough to register readily the blood flow even of a small toe in all its detail. This is of clinical importance since pathologic processes may either pick out a single digital artery or affect them all in varying degrees. In the case of the toes, particularly the big toe, the plethysmograph necessarily is sealed just proximal to the interphalangeal joint. It therefore encloses skin covering mainly the end phalanx. The latter, however, contains a vast amount of arteriovenous anastomoses, and thus has a considerably greater blood flow than the skin of the proximal phalanges which show only a few of these structures. Thus, strictly speaking, the plethysmogram of the big toe can be compared with that of the finger tip only.

1. The Height of the Pulse Volume: All other factors being equal, the height of the pulse volume depends upon the amount of tissue enclosed within the plethysmograph. Therefore differences in the height of the pulse volume must be expected in various subjects and, for this reason, the recorded height of the pulse volume is not a strictly comparable index of the circulation. Comparable indices are, however, easily obtained by correcting the height of the pulse volume to a mean digital volume (conveniently 15 c.c.) by means of the simple formula:

$$\text{Pulse volume (corrected)} = \frac{\text{Pulse volume (recorded)} \times 15}{\text{Digital volume in cubic centimeters}}$$

Thus, the corrected pulse volume of a very big first toe of 30 c.c. tissue volume which records a pulse volume of 0.04 c.c. is the same as that of a small toe of 7.5 c.c. which records a pulse volume of only 0.01 c.c., i.e., 0.02 cubic centimeters. While this is the correct procedure, it complicates the issue. For all practical purposes, however, it is sufficient, according to my experience, to compare the uncorrected height of the pulse volume of respective toes in various subjects if the above point is kept in mind. Therefore all our values refer to the uncorrected pulse volume of the big toe unless otherwise stated.

Fig. 2.—The pulse volume of a normal subject at various states of vasomotor tone. *A*, Moderately constricted, first left toe; skin temperature, 26° C. *B*, Moderately dilated, first left toe; skin temperature, 30° C. *C*, Fully dilated, first left toe; skin temperature, 35° C. *D*, Fully dilated, second left toe; skin temperature, 34.3° C. Room temperature, 21° C. Reduction of original tracings to two-thirds.

All tracings were obtained in reclining position unless otherwise stated, and in all the following abbreviations have been used:

P = pressure in cuff during venous congestion test; *P.V.* = pulse volume; *R* = respiratory movements (arrow indicates inspiration); *S* = signal; *S.G.* = sphygmogram of arteria dorsalis pedis; *Sk.T.* = skin temperature; ordinates in all tracings = two seconds; white horizontal line = calibration for pulse volume and digital volume. Change from line to line equals 0.01 cubic centimeter.

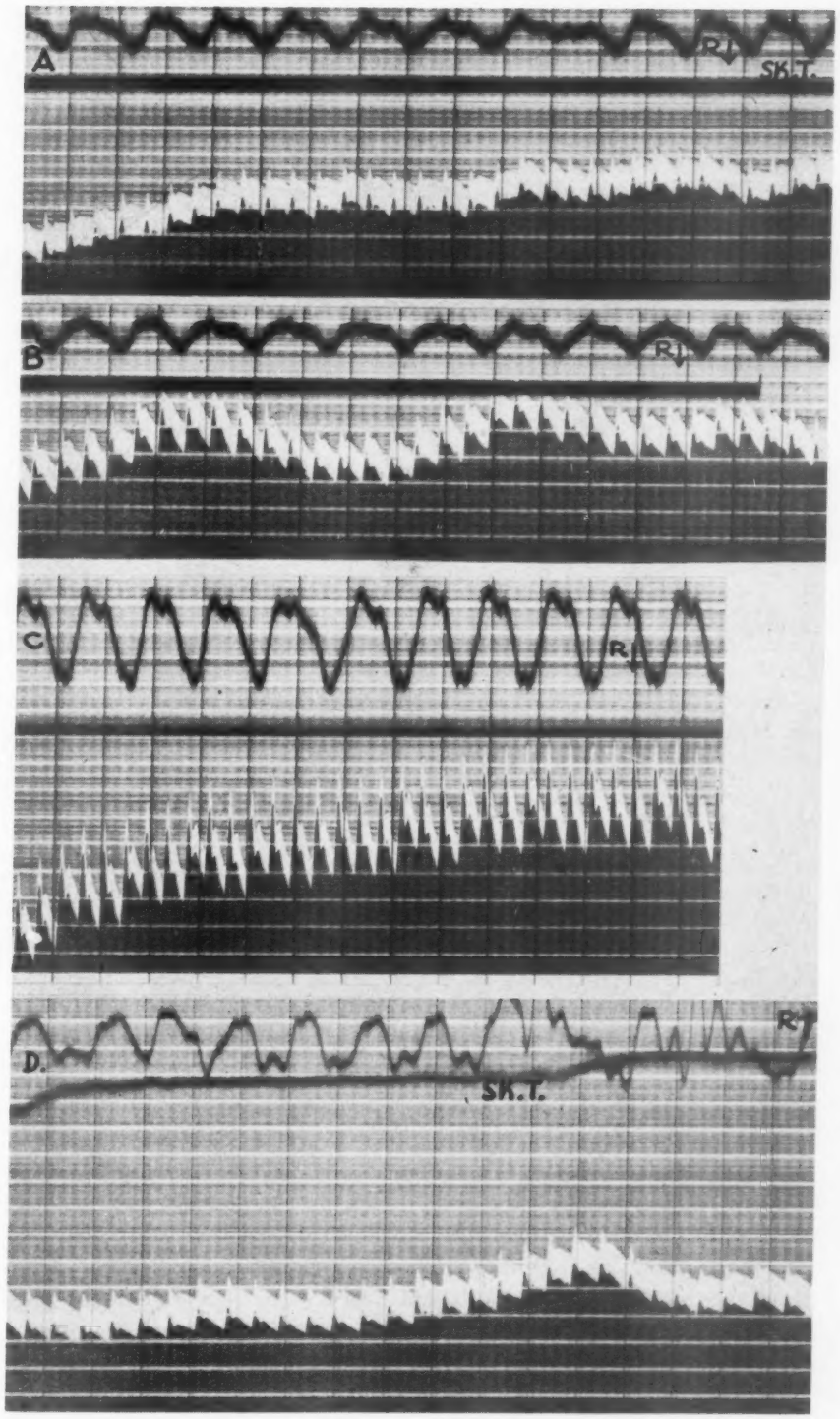

Fig. 2.—*(For legend see opposite page.)*

The height of the pulse volume in a normal subject is dependent upon the vasomotor tone (Figs. 2 and 10). As a rule it varies between 0.002 c.c. during maximum constriction and 0.025 c.c. during full dilatation. Occasionally, in younger subjects, values up to 0.045 c.c. are met with, while in others, particularly older subjects without clinical signs of arterial disease, the pulse volume during full dilatation may not exceed 0.020 cubic centimeters. Due to the smaller amount of tissue enclosed, the recorded pulse volume of a small toe reaches about 0.01 c.c. only during full dilatation (Fig. 2, *D*).

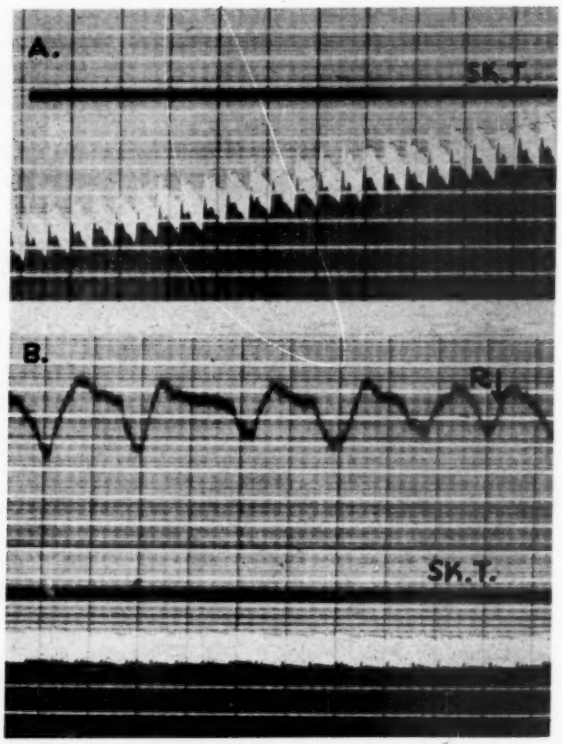

Fig. 3.—Pulse volume of a normal subject demonstrating difference between vasomotor tone of upper and lower extremities. *A*, Third left finger showing moderate dilatation. Skin temperature, 31° C. *B*, First left toe, taken immediately afterwards but showing full constriction. Skin temperature 23° C. Room temperature 22° C. For abbreviations, consult legend to Fig. 2. Reduction of original tracings to two-thirds.

As previously indicated[23] the vessels of the fingers under basal conditions and at room temperatures of 20° to 23° C. are usually neither constricted nor fully dilated but assume a value intermediate between these extremes, allowing adjustment according to the needs of body temperature regulation. The pulse volume of the toes in the same subjects, however, is as a rule found near the lower limit of normality under similar circumstances, the vessels often being actually maximally constricted even in "warm-handed" subjects (Fig. 3). This indicates that the vasomotor tone of the blood vessels of the lower extremities is considerably higher than that of the fingers. In "cold-handed" subjects

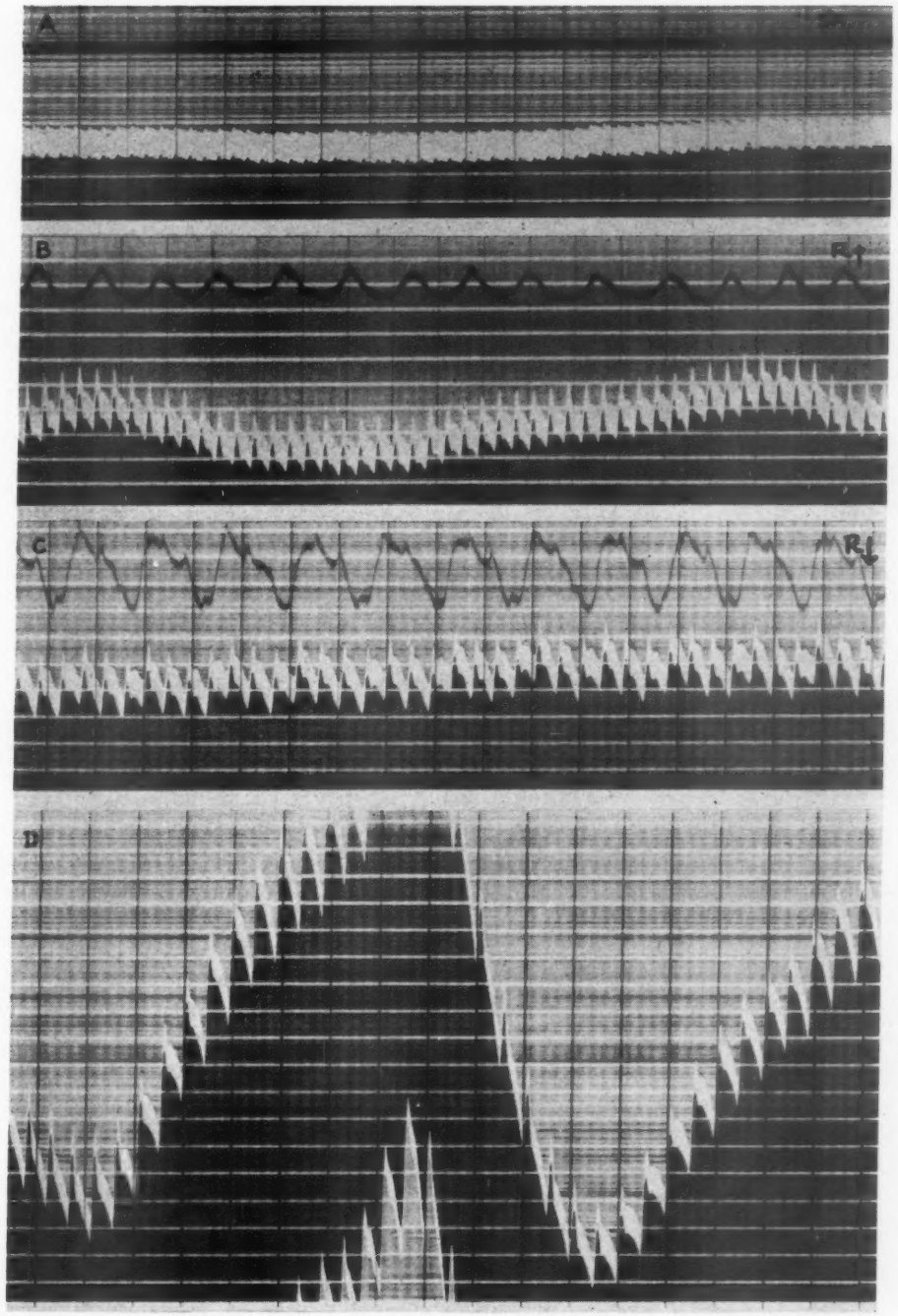

Fig. 4.—Spontaneous fluctuations in pulse and digital volume. *A*, Normal subject (first left toe) during rest. High vasomotor tone. Skin temperature 22.8° C. *B*, Normal, subject (first left toe) moderately dilated. Skin temperature 31° C. *C*, Absence of spontaneous fluctuations following lumbar ganglionectomy (first right toe). Skin temperature 34° C. *D*, Normal subject fully dilated but elevated (first left toe). Skin temperature 34.5° C. Reduction of original tracings to two-thirds. Room temperature 23° C. For abbreviations, etc., consult legend to Fig. 2.

without clinical signs of arterial disease, the vessels, when tested under the same conditions, are invariably fully constricted, the pulse volume being rarely higher than 0.002 cubic centimeter.

2. Fluctuations in the Height of the Pulse Volume: The height of the pulse volume of the fingers has been found to be in a state of continuous rhythmic fluctuation which is abolished by the interruption of the sympathetic pathways (Goetz[23]). It therefore reflects the rhythmic fluctuating nature of sympathetic activity. Indeed, the pulse volume is an exquisite indicator of that vasomotor activity which is of insufficient degree to show itself in blood pressure changes. However, in the lower extremities during rest these fluctuations of the pulse volume are either absent or very shallow (Fig. 4, *A*) on account of the high vasomotor tone just demonstrated. As the vasomotor tone of the toe vessels diminishes during body heating and the pulse volume rises, fluctuations become registrable (Fig. 4, *B*). They are extremely prominent in the elevated limb but shallow during dependency, which is particularly obvious during full dilatation when, in the elevated limb, the fluctuations are at their maximum (Fig. 4, *D*).

Naturally, the plethysmogram reflects all known variations in shape and rhythm of the sphygmogram. A Corrigan or water-hammer pulse, pulsus alternans, pulsus bigeminus, arrhythmias, and the like, are easily demonstrated (Fig. 5). Of particular interest are the changes in the pattern demonstrated in Fig. 5, *D*, which are due to changes in the character of the blood pressure occurring during artificially induced hypoglycemic shock. As is well known, the blood and pulse pressures rise during hypoglycemia; this is well reflected in the changes in the pattern of the pulse volume, particularly in the disappearance of the dicrotic wave.

3. Fluctuations in Digital Volume: The plethysmogram does not, as a rule, move along a straight line but fluctuations occur which indicate changes in toe volume (Fig. 4). These volume changes correspond to, and are mainly the result of, fluctuations in the height of the pulse volume. Consequently, spontaneous changes in digital volume are less prominent in the toes than in the fingers on account of the higher vasomotor tone in the former (Fig. 4, *A*), but they become equally marked as the vasomotor tone is relaxed (Fig. 4, *B*). These changes assume considerable proportions in the elevated limb (Fig. 4, *D*) and are very less marked during dependency. Like the changes in pulse volume, they are dependent upon the integrity of the sympathetic nervous system and therefore are absent following ganglionectomy (Fig. 4, *C*).

Abramson and Katzenstein,[2] using their foot plethysmograph, reported that spontaneous fluctuations in blood flow were characteristic for the hand, but in

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Fig. 5.—Changes in shape and rhythm of pulse volume. *A*, In auricular fibrillation (first left toe). Skin temperature 33° C. *B*, Interpolated extra systoles (first right toe). Skin temperature 31.3° C. *C*, Dropped beats (first left toe). Fully dilated Skin temperature 35° C. *D*, Change in shape with change in blood pressure (first left toe). (a) During rest. B. P. 110/75. Skin temperature 36° C. (b) During artificial hypoglycemia. B. P. 150/50. Skin temperature 36° C. *E*, Pulsus bigeminus (first right toe). Skin temperature 33.7° C. Reduction of original tracings to two-thirds. Room temperature 23° C. For abbreviations, etc., consult legend to Fig. 2.

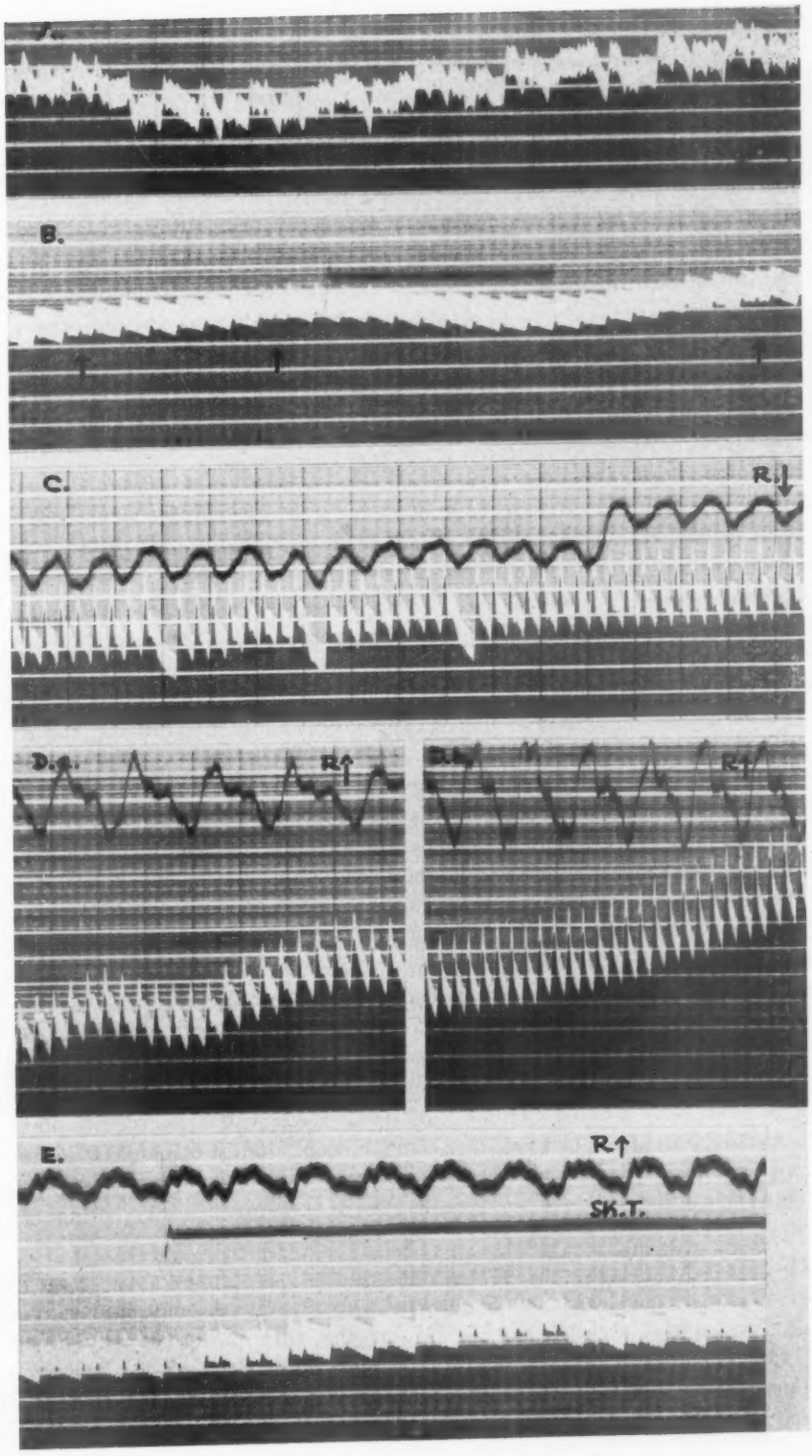

Fig. 5.—*(For legend see opposite page.)*

the foot they were either "absent or insignificant." Obviously in these authors' experiments the feet, in contrast to the hands, were tested during dependency, which, in the light of the above data, easily explains their failure to demonstrate spontaneous fluctuations. There can be no doubt from our investigations that, in the lower extremities, spontaneous fluctuations do occur in the same degree as in the upper extremities, if tested under identical conditions, which include identical hemostatic conditions as expressed by posture.

Spontaneous fluctuations in the toe volume are less pronounced during the venous congestion which is obtained from inflating to 60 mm. Hg a cuff fixed at the ankle. Nevertheless, they are still obtained (Fig. 8, *B*). This is evidence that the fluctuations are mainly the result of changes in arterial inflow since, according to Lewis,[33] both veins and capillaries are unable to constrict against the pressure used.

Ever since the first description of plethysmographs, changes occurring simultaneously with the respiration have been described, the true vasomotor nature of which has been maintained by some and doubted by others. Unless there was pronounced cardiac respiratory arrhythmia, changes in the toe volume resulting from the normal respiration were hardly ever prominent in our tracings.

In our earlier communications we described how a single deep inspiration, imitative of a sigh, or a series of deep breaths regularly produced peripheral constriction in the fingers, the degree depending upon the tone of the digital vessels.[19, 20] This fact since has been amply confirmed by numerous authors. The vessels of the toes are affected by this constriction to the same degree (Fig. 6, *A*), and the reaction shows all the characteristics described elsewhere.[20, 23] This constriction is set in train only by the inspiratory phase, and since it is not obtained following lumbar ganglionectomy (Fig. 6, *D*) it is dependent upon the integrity of the sympathetic pathways and is thus a true vasoconstrictor reflex. When moderately or fully dilated the reaction is easily recorded, but under ordinary conditions the reaction may be absent because of the already high vasomotor tone. Indeed, even a slight increase may be obtained instead of the usual fall (Fig. 6, *B*). Thus Peters,[35] using our method, did not obtain vasoconstriction in the one subject tested by him. His Fig. 12 is strikingly similar to our Fig. 6, *B*. The decrease in digital volume following a deep breath is extremely pronounced in the elevated leg when the venous plexus is empty and well drained (Fig. 6, *C*). Under such conditions constriction of the veins could hardly account for such a marked volume decrease. The constrictor reflex following a deep breath affects therefore mainly, if not solely, the arteries.

The effects of various sensory stimuli (e.g., an unexpected noise [Fig. 7, *A*], application of cold or pain, single or multiple principles, emotional content of thought or mental strain [Fig. 7, *B*], or the anticipation of any of these) upon the peripheral circulation were tested and they always resulted in vasoconstriction. All of these are well-known vasoconstrictor reflexes and as such are not obtained after ganglionectomy (Fig. 7, *C*). A similar con-

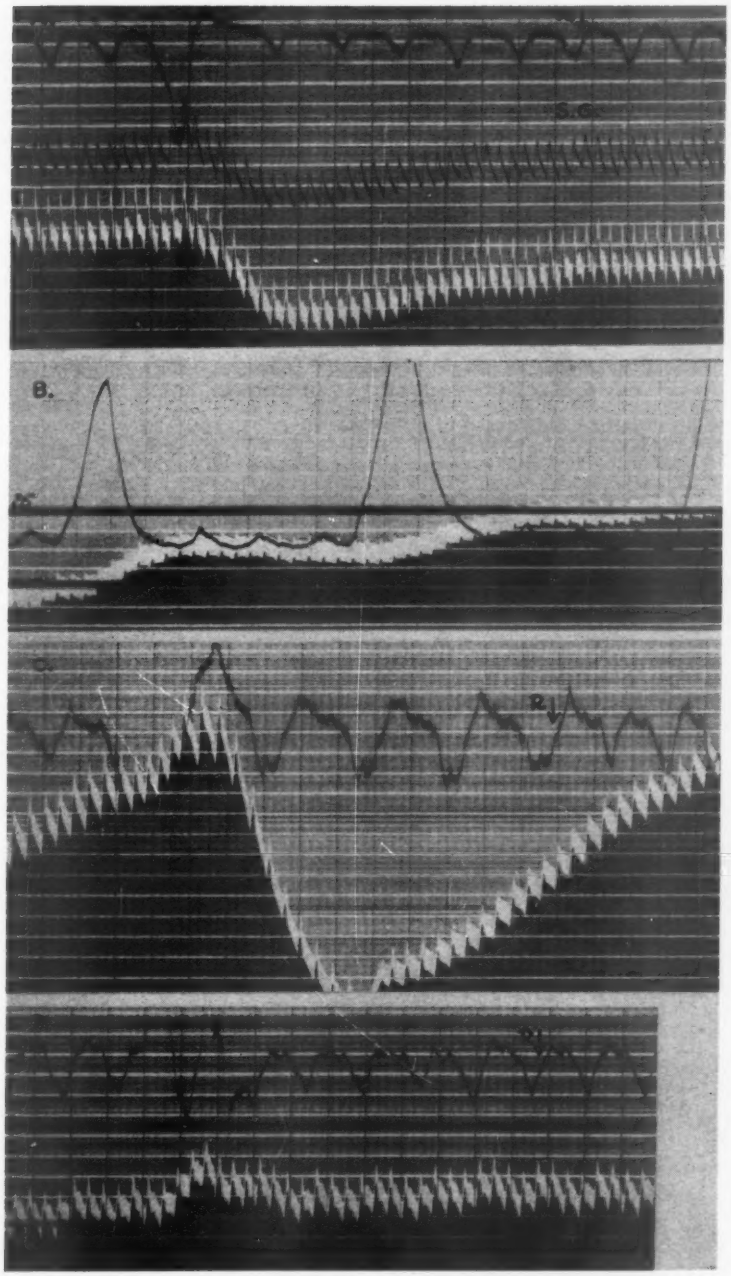

Fig. 6.—Effect of a deep inspiration upon blood flow through toe. *A*, Normal individual (first left toe) fully dilated. Skin temperature 32° C. *B*, Normal individual (first left toe) constricted. Skin temperature 26° C. *C*, Normal individual (first left toe elevated). Skin temperature 34° C. *D*, No response in sympathectomized extremity (nine years previously). Skin temperature 34° C. Reduction of original tracings to one-half. Room temperature 23° C. For abbreviations, etc., consult legend to Fig. 2.

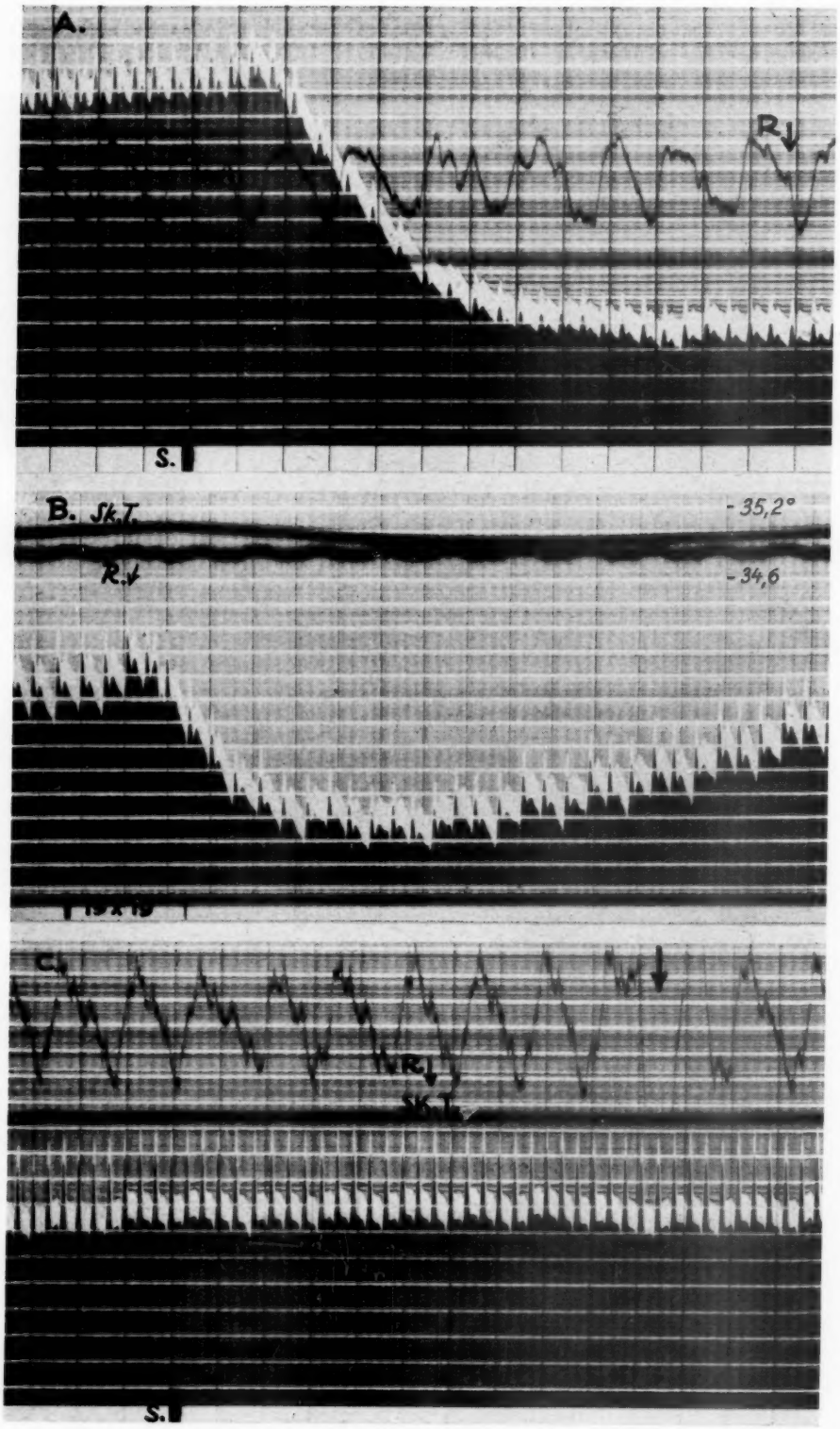

Fig. 7.—*(For legend see opposite page.)*

strictor reflex results from sudden inflation of a blood pressure cuff (Fig. 8, *A*). This may raise the systolic blood pressure by as much as 15 mm. of mercury. The clinical importance of such a reflex as regards the accuracy of blood pressure readings is worthy of further study. The diminution in digital volume from any of the constrictor reflexes just mentioned is greater in the elevated limb than in the dependent one for reasons mentioned previously, which suggests that the constriction is arterial rather than venous, in contrast to the opinion of some authors.[2, 9]

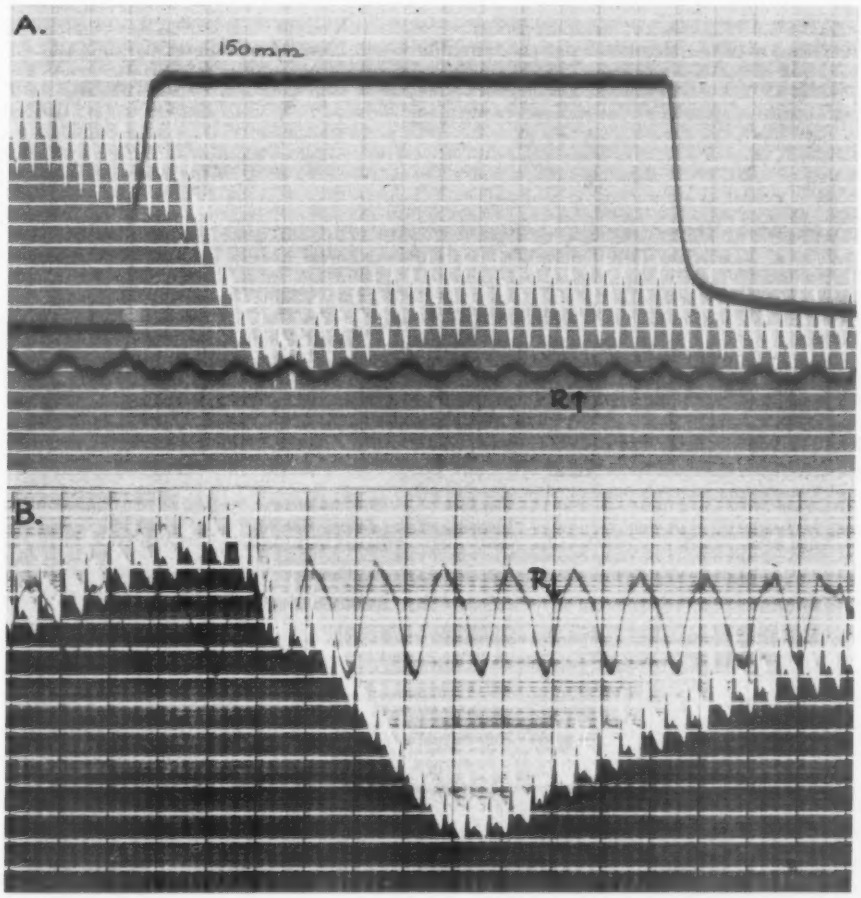

Fig. 8.—*A*, Effect of interruption of blood flow in an upper extremity upon blood flow through toe (first left toe). *B*, Fluctuations in blood flow occurring during venous congestion of 60 mm. Hg (first right toe). Reduction of original tracings to two-thirds. For abbreviations, etc., consult legend to Fig. 2.

Fig. 7.—Effect of unexpected noise (*A*) and mental strain (*B*) on blood flow through toe. Between the signals in (*B*) the subject was calculating the problem 19 × 19. *C*, No effect in sympathectomized extremity (ten years previously). First left toe. At the arrow, accidental deep breath. Reduction of original tracings to two-thirds. Signal in *A* and *C*: unexpected noise. For abbreviations, etc., consult legend to Fig. 2.

*B. The Rate of Blood Flow in the Toes.**—

1. Calculation of the Rate of Blood Flow: The venous congestion test previously described in detail[23] was employed to calculate the rate of blood flow in the toes. In brief, the rate of blood flow was determined by stopping the venous return from the toes by means of a blood pressure cuff fixed at the ankle, without impeding the arterial inflow. A normal tracing (Fig. 9, *A*) takes the following characteristic course: (a) it rises along a straight line, following this, (b) it slopes gradually until the vascular bed is filled, when (c) it runs parallel to the base line. When the pressure is released the tracing returns to the initial level, as a rule to within hundredths of a cubic centimeter. During the first part the volume increase per second is read; this serves as a measure of the arterial inflow. The rate of blood flow is then calculated per minute and for 100 c.c. of tissue from the following formula:

$$R = k \frac{I \times 100 \times 60}{V}$$

wherein: R = Rate of blood flow in cubic centimeters per minute.
k = Factor which is constant for a particular site of the cuff; e.g., k = 3 if the cuff is fixed at the ankle (see second paragraph below).
I = Increase in digital volume per second in cubic centimeters.
V = Digital volume in cubic centimeters.

The results obtained with this method are very consistent and enable evaluation with great accuracy as long as the pressure of the cuff is well below the diastolic pressure. However, pressures below 30 mm. Hg are apt to give erroneous results.

The site of the congesting cuff is of importance for the correct calculation of the rate of blood flow. If two cuffs are fixed on the same leg, one being below the knee and the other at the ankle, the inflow tracing obtained in the latter case is steeper than that in the former. This difference in the gradient appears to be due to the difference in the amount of the venous network distal to the cuff. Therefore, for the correct measurement of the arterial inflow the cuff should be fixed at the base of the digit. In the case of the toes, however, this is impossible, and we have to apply the cuff at the ankle.

It had been found for the fingers[23] that the increase in volume per second from venous congestion applied at the basal phalanx was three times that obtained from congestion applied at the wrist. If we assume that the same relations exist in the foot, then we could assume that the increase in toe volume from venous congestion applied at the base of the toe would also be three times greater than that obtained from congestion applied at the ankle. Therefore the results obtained from congestion applied at the ankle have to be multiplied by three—the factor k in our formula—in order to obtain the actual rate of blood flow.

Following the release of the venous congestion the volume returns, as a rule, to the original level (Fig. 9, *A*). However, in some subjects a fall below

*The results refer to tests carried out with the patient in the reclining position.

the latter occurs, and it is immediately followed by a rise to the initial level (Fig. 9, *B*). Abramson and his coworkers,[4] who also observed this phenomenon, took it for a reflex mechanism. Fig. 9, *B*, which was obtained in a patient with lumbar sympathectomy proves that, if this is a reflex, it cannot be a spinal sympathetic one.

2. Changes in the Rate of Blood Flow: The rate of blood flow fluctuates in accordance with changes in the height of the pulse volume which, as we have seen, in turn depends upon the vasomotor tone. The higher the pulse volume, the greater the gradient and the greater the rate of blood flow (Fig. 10). The rate of blood flow to the toes of normal subjects thus calculated varied between

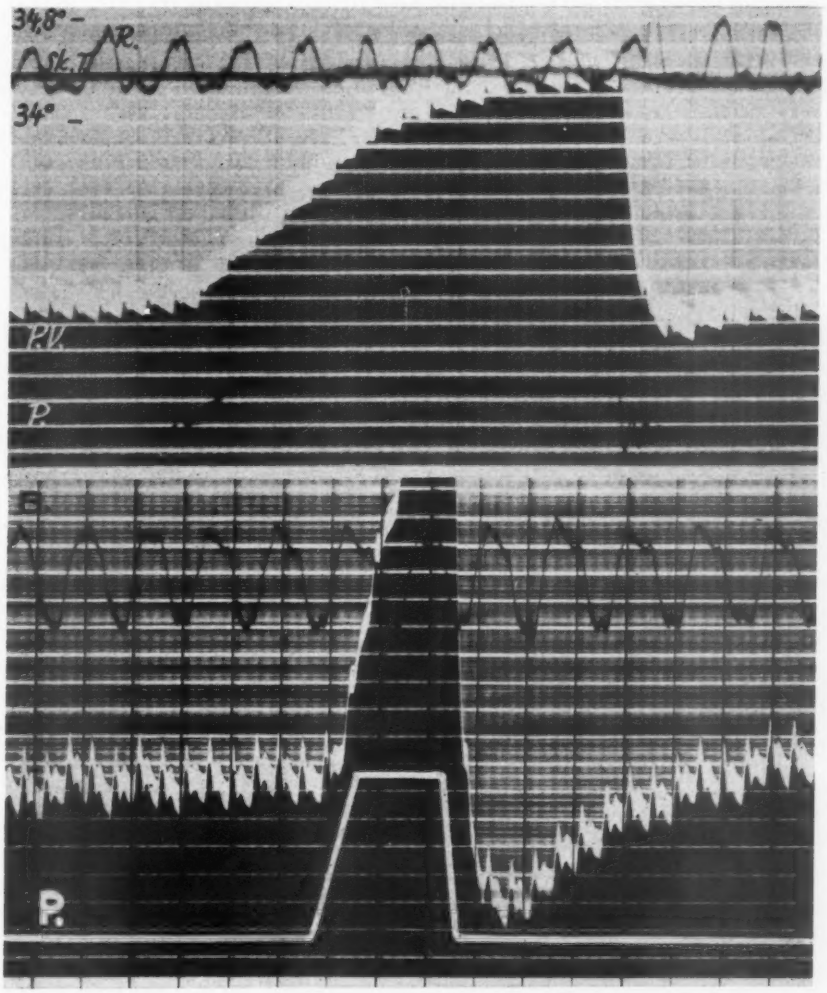

Fig. 9.—*A*, Typical tracing of venous congestion test (second left toe, fully dilated). Note initial rise along straight line and return to initial level with release of pressure. Skin temperature ±34° C. Room temperature 21° C. *B*, Venous congestion test (first right toe, sympathectomized) showing transient fall below base line with release of pressure. Skin temperature 34° C. Room temperature 23° C. Record of pressure has been retouched with white. Cuff applied at ankle in all tracings unless otherwise stated. Reduction of original tracings to two-thirds. For abbreviations, etc., consult legend to Fig. 2.

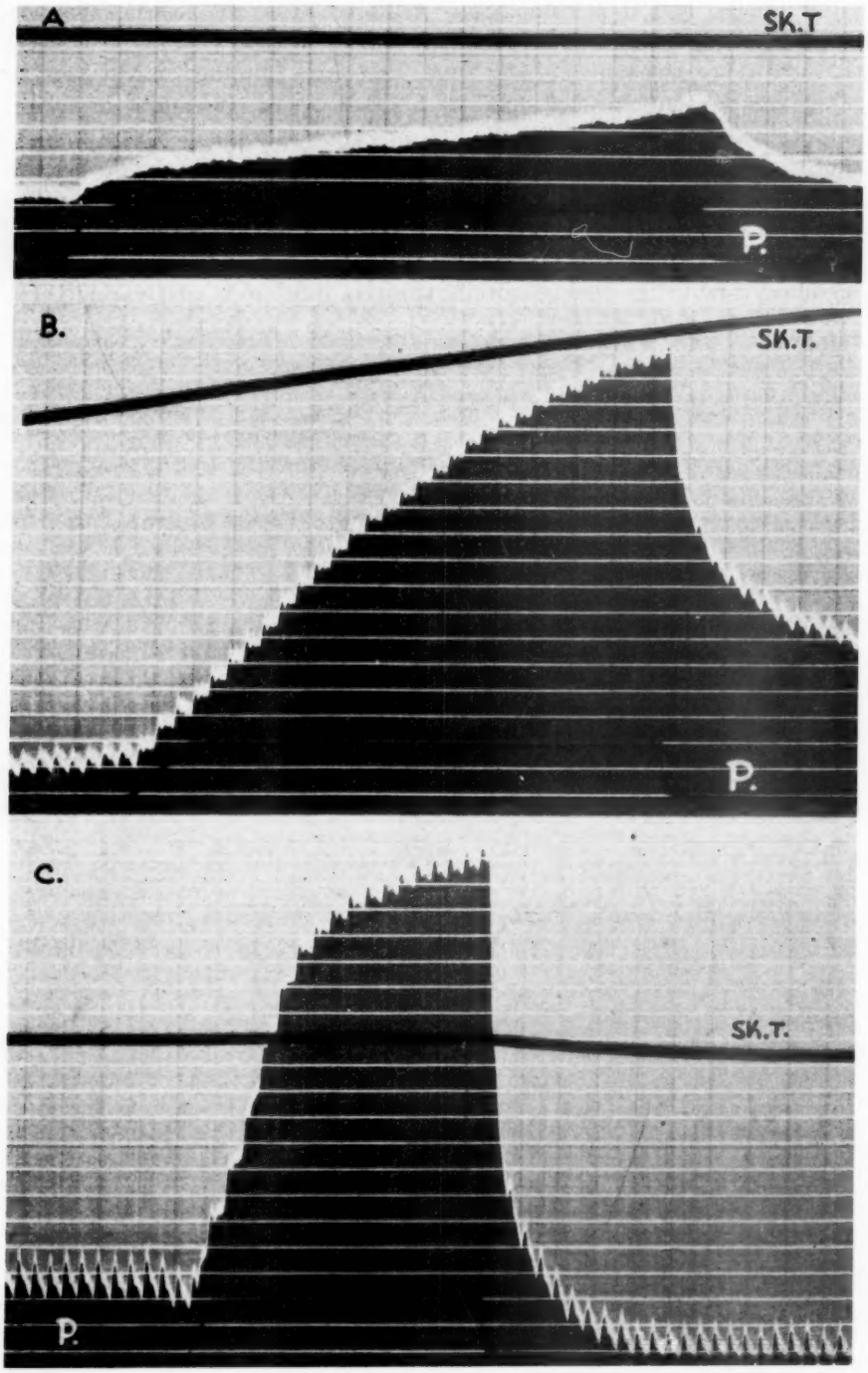

Fig. 10.—Effect of vasomotor tone on gradient of rise during the venous congestion test (first left toe). *A*, Full constriction; skin temperature 22° C. *B*, During dilatation, skin temperature ±25° C. *C*, Almost fully dilated, skin temperature 34.9° C. Room temperature 21° C. Reduction of original tracings to two-thirds. For abbreviations, etc., consult legend to Fig. 2.

1 c.c. during full constriction and 90 c.c. per minute for 100 c.c. of tissue when fully dilated. These values compare very well with those obtained for the skin of the fingers, but are considerably higher than those calculated by Kunkel and Stead[30] for the foot.

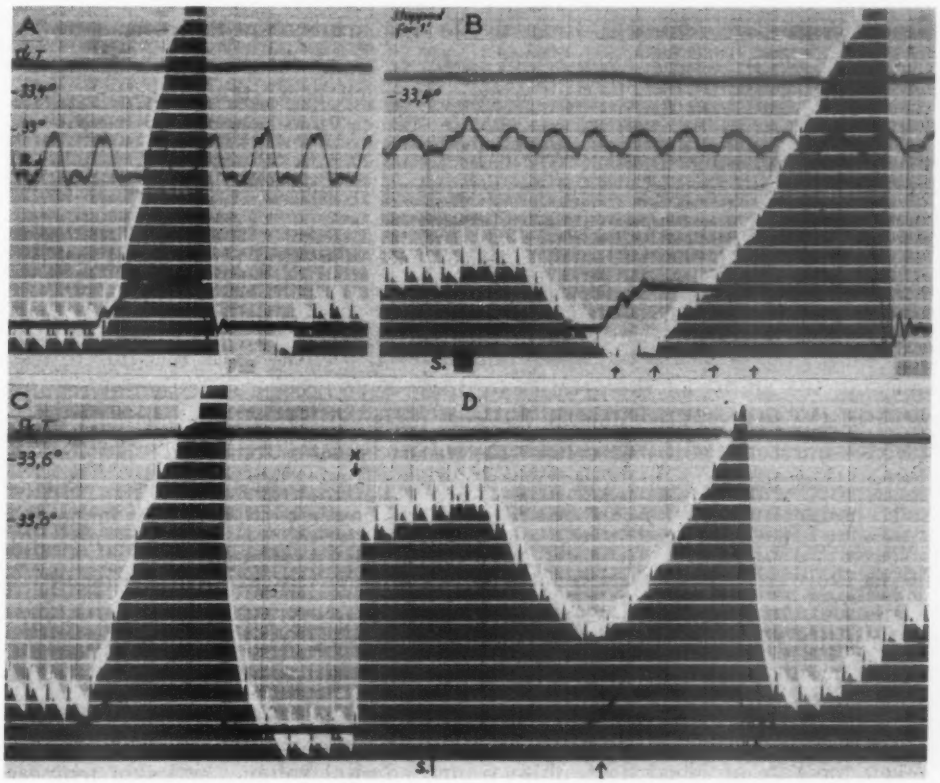

Fig. 11.—*A* and *B*, Effect of unexpected noise upon blood flow through toe (first left toe). Explanation in text. *C* and *D*, Effect of deep breath upon rate of blood flow through toe (first left toe). Cuff applied below knee. Explanation in text. Reduction of original tracings to two-thirds. At *X* adjustment of plethysmogram. For abbreviations, etc., consult legend to Fig. 2.

The changes in the rate of blood flow which result from reflex constriction, such as an unexpected noise or a deep breath, are illustrated by Fig. 11. In Fig. 11, *A*, venous congestion was applied during complete relaxation, the rate being 42 c.c. per minute for 100 c.c. of tissue. One minute later, at the signal (Fig. 11, *B*), an unexpected noise was made and peripheral constriction resulted. The pulse volume decreased from 0.022 to 0.01 cubic centimeter. Eight seconds later, at the height of the response, the venous return was arrested by the same pressure as was applied in Fig. 11, *A*. On account of the preceding vasoconstriction the increase in volume was less steep. In addition, the tracing is altogether differently shaped. It slopes upward. This is very similar in all tracings, and appears adequately to be explained by the wearing off of the constriction resulting in an increased arterial inflow with every consecutive heart-

beat. Thus the rate of blood flow calculated during the first two pulses is about 4.5 c.c. per minute, for the next three pulses it is 9 c.c., and it is 12 c.c. between the third and fourth arrows. From the fourth arrow onward, the rate of blood flow is 16.5 cubic centimeters.

Similarly, the constriction resulting from a deep inspiration can be analyzed (Fig. 11, *C* and *D*). Prior to the deep inspiration the blood flow was 50 c.c. per minute and for 100 c.c. of tissue (Fig. 11, *C*). At the height of the reflex constriction (Fig. 11, *D*) the rates of blood flow, starting at the arrow, were calculated as follows: 4 c.c., 12 c.c., 20 c.c., and, eventually, 30 c.c. per minute for 100 c.c. of tissue. When the pressure was released, the volume fell markedly below the initial level but rose immediately afterward. It was only then that the constriction wore off completely.

The effect of a chain of such constrictor impulses and the effect of smoking upon the peripheral blood flow have already been dealt with elsewhere.[22]

C. The Effect of Body Heating.—Ever since the clinical importance of differentiating between arterial spasm and arterial occlusion was recognized, tests assessing the ability of the arteries to dilate have become an essential requirement in the study of peripheral vascular diseases. Of all the methods which have been recommended to relieve the vasoconstrictor tone, body heating has proved least objectionable and very satisfactory for clinical purposes. Gibbon and Landis[18] produced reflex dilatation in the lower extremities by immersing both forearms in water to 42° to 45° C. They tried immersion of one hand as far as the wrist but this did not result in complete relaxation of the blood vessels of the feet. However, according to our experience, complete vasodilatation will readily result from immersion of *one* arm to a point about 5 to 7 inches above the elbow, provided the subject is covered with a woollen blanket to prevent the dissipation of heat.

Fig. 12 represents a typical response as obtained in a normal subject. When the rate of blood flow, pulse volume, digital volume, and skin temperature are recorded simultaneously it can be seen that pulse volume and digital volume are the first to rise after a small initial drop. It is only after the blood flow has been increasing for some time that the skin temperature starts rising. In our case both pulse volume and rate of blood flow reached their maximum dilatation level after twelve minutes. Digital volume and skin temperature, however, continued to rise for eight more minutes. The relation between the height of the pulse volume and the rate of blood flow, on the one hand, and the skin temperature on the other can be clearly appreciated, and it is obvious that the pulse volume furnishes the clearest picture of the state of the circulation at any one moment. In this person reflex dilatation occurred very rapidly since there was moderate dilatation at the outset. With vessels fully constricted there is, however, considerable delay, and dilatation often does not commence for eight to ten minutes.

In the opinion of Gibbon and Landis a normal response to body heating, that is, a rise in skin temperature to 32° C. or above within thirty to thirty-five minutes, "definitely excludes the possibility of obliterative structural disease of

the arteries as a cause of the diminished blood flow in the lower extremities."[32] This statement has been generally accepted, and skin temperature measurements have accordingly been evaluated for assessing the efficiency of the arterial circulation. However, on numerous occasions we have observed that the skin temperature reached the normal vasodilatation level (32° C.) within thirty minutes, yet the height of the pulse volume and the rate of blood flow remained

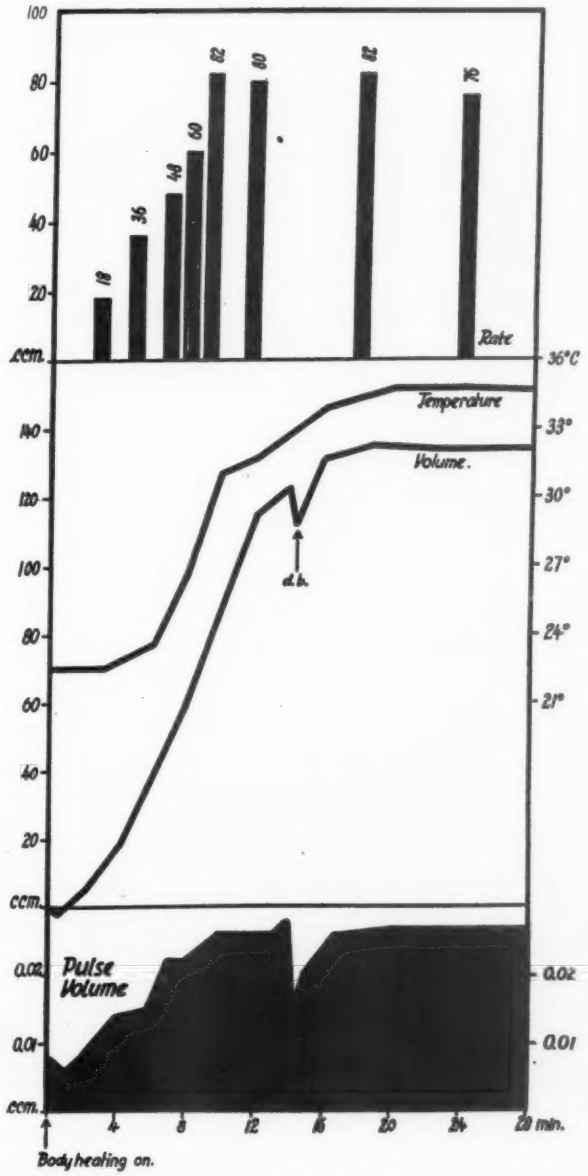

Fig. 12.—Effect of body heating upon the pulse volume, digital volume, skin temperature, and the rate of blood flow through the toe of a normal subject, all continuously recorded (first left toe). Room temperature 21° C.

considerably below the values seen normally during full vasodilatation (Fig. 13). Pulse volume and rate of blood flow therefore indicated organic vascular disease, whereas the skin temperature did not suggest this. Direct application of heat and paravertebral block did not furnish a higher pulse volume than did body heating. Fig. 14 shows the results of testing one of the arteries of the

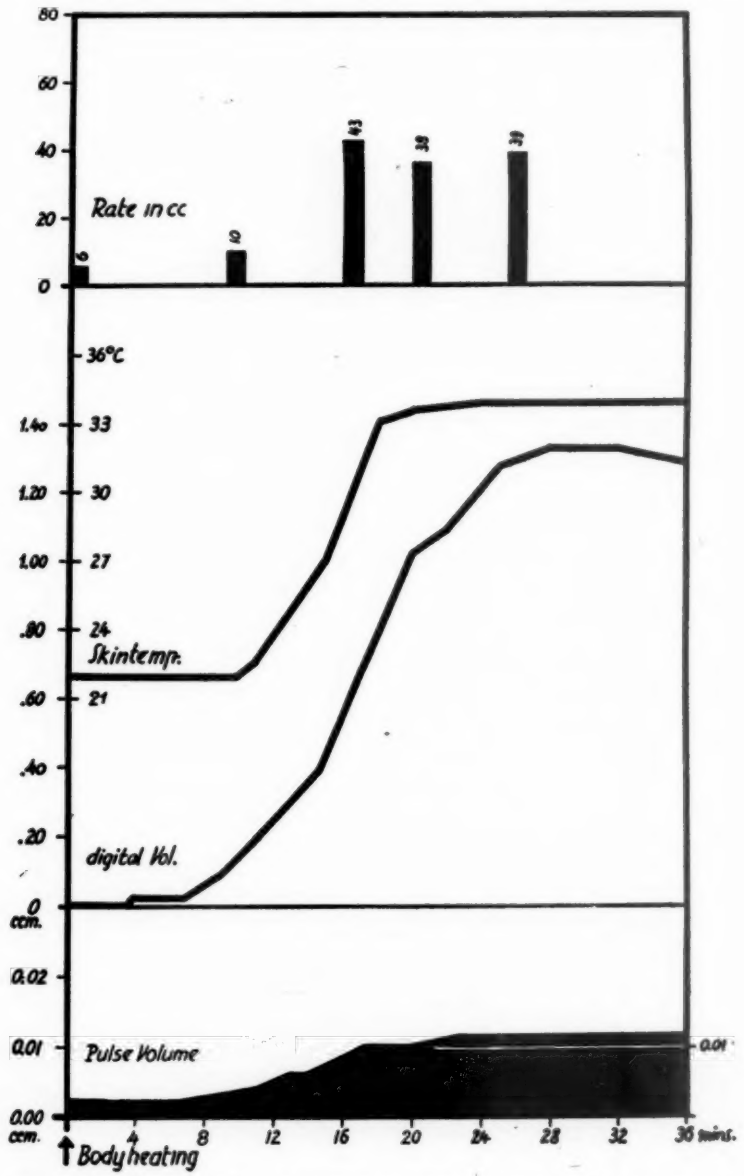

Fig. 13.—Effect of body heating upon pulse volume, digital volume, skin temperature, and rate of blood flow in a digit with moderate organic occlusion. Note normal response in skin temperature but decrease in pulse volume and rate of blood flow during full dilatation. Room temperature 21° C.

digit. There is no doubt that structural changes were responsible for the diminished pulse volume. These findings therefore illustrate two points: (1) a rise in skin temperature to the normal vasodilatation level in response to body heating does not exclude organic obstruction, and (2) digital plethysmography is capable of demonstrating structural changes in arteries at a stage when the skin temperature measurement is unable to detect them.

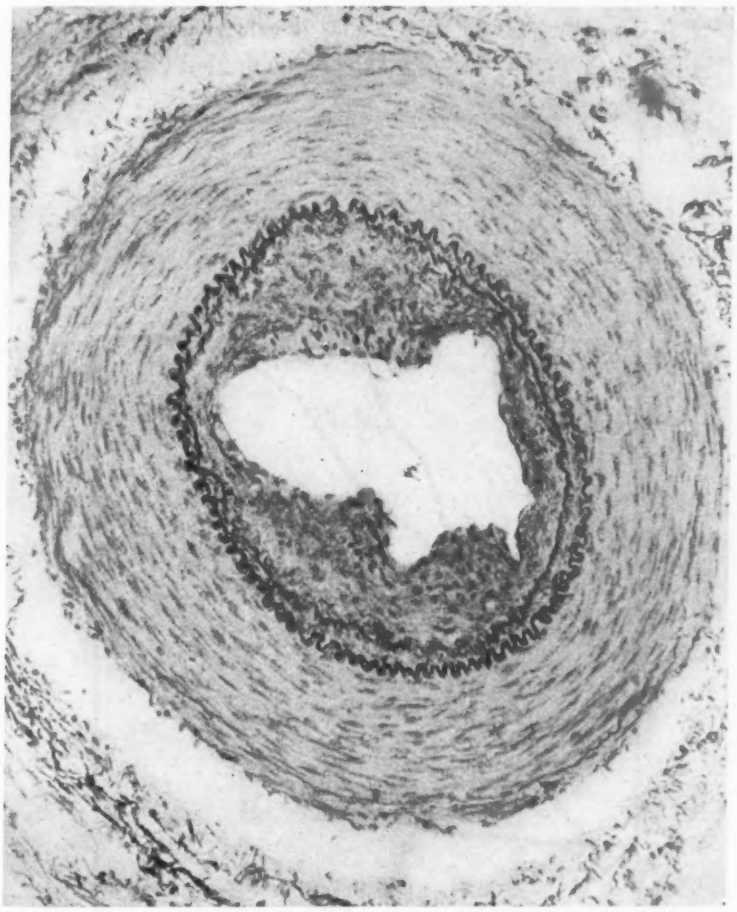

Fig. 14.—One of the arteries of digit examined in Fig. 13.

It has been generally accepted that vasodilatation induced in one extremity by warming another depends upon the return of warmed blood to the general circulation affecting the temperature-regulating center in the hypothalamus.[17] However, Uprus, Gaylor, and Carmichael[44] pointed out that it is the gradient or steepness of the rise in blood temperature, rather than the actual temperature of the blood, which initiates reflex vasodilatation. We found that recognition of the latter fact is of great clinical importance because it constitutes a source of error in the immersion method hitherto not stressed. Obviously, in order to

obtain a sufficient gradient, the blood flow through the immersed extremity should be normal, otherwise little warmed blood will be returned. If the arteries of the immersed arm are partially or totally occluded, the blood will warm only very slowly and a slow gradient will result. Reflex dilatation may thus fail or be incomplete, and an organic occlusion may be simulated in an extremity where the blood flow is actually normal (Fig. 15). In such a case the diminished reflex dilatation is the result of organic occlusion of the vessels of the immersed extremity and not of the tested one, as can be proved by immersing another extremity whereupon a normal response is obtained (Fig. 15).

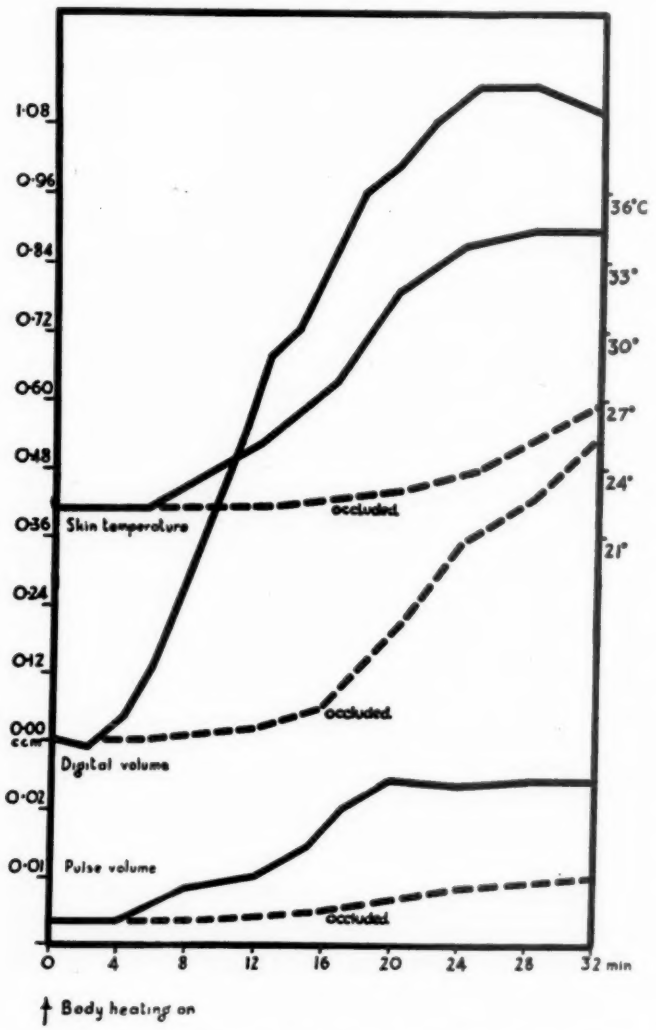

Fig. 15.—Effect of body heating resulting from immersion of an extremity with patent (black lines) and with markedly occluded arteries (interrupted lines) upon the blood flow through an extremity with normal arterial circulation. Room temperature 21° C.

Pickering and Hess[37] have already noted that body heating may not be an adequate procedure to dilate the vessels in the lower extremities of some normal subjects. In our series we had two subjects who were free from clinical signs of spastic vascular disease, such as Raynaud's phenomenon or acrocyanosis, but always had noticed that their extremities were cold and clammy.* Like

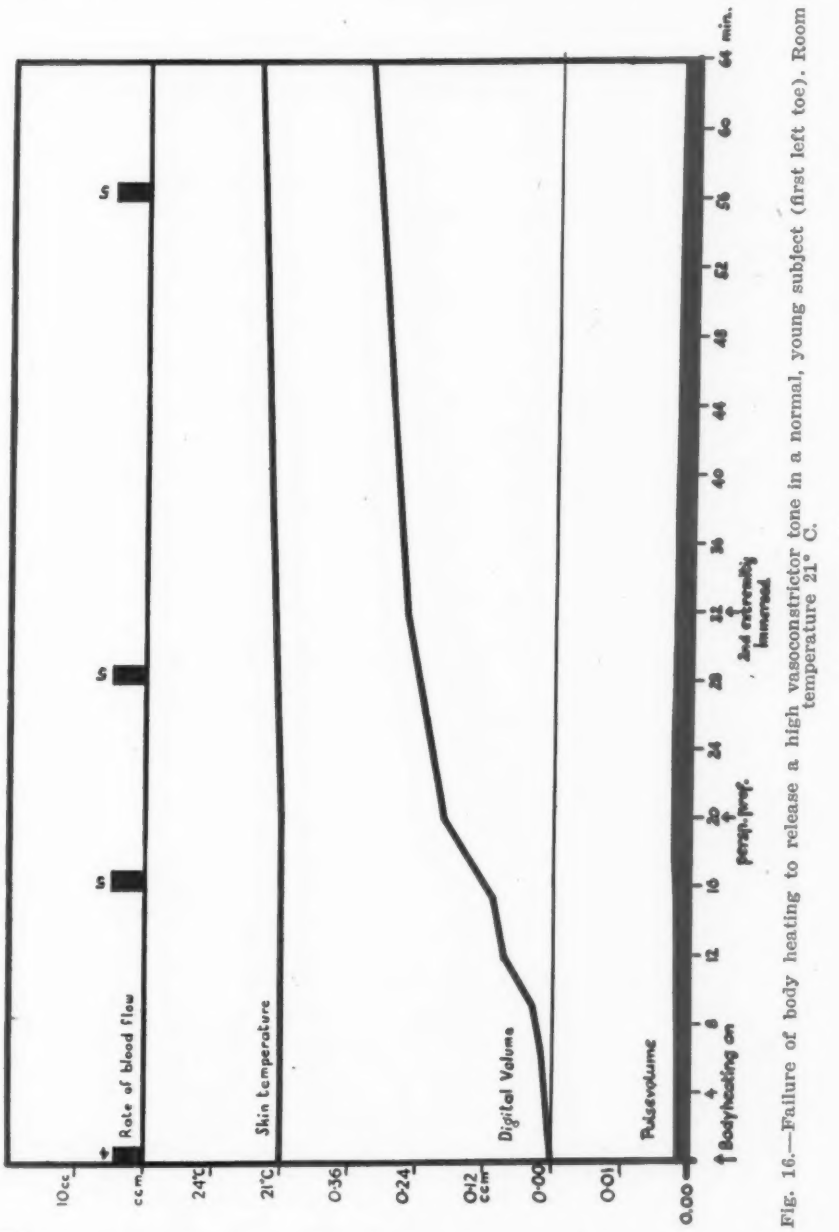

Fig. 16.—Failure of body heating to release a high vasoconstrictor tone in a normal, young subject (first left toe). Room temperature 21° C.

*It may be of significance that in one of them a suprarenal rest was found on operation for inguinal hernia.

all other persons they started to perspire profusely after twenty minutes' body heating, yet there was hardly any change in pulse volume, digital volume, or skin temperature within thirty minutes (Fig. 16). Immersion of an additional extremity for another thirty minutes did not produce the desired relaxation. Following the local application of heat, prompt relaxation of the vessels was obtained. The pulse volume rose to 0.025 c.c. (Fig. 17), and the rate of blood flow was 80 c.c., indicating that we were not dealing with an organic occlusion but a high vasomotor tone.

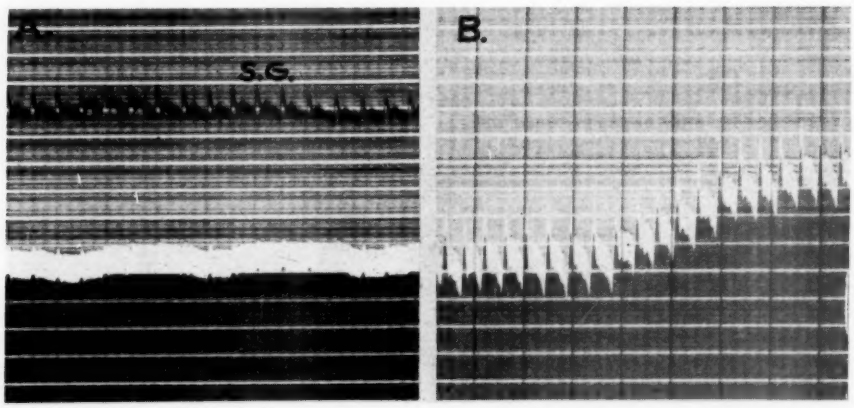

Fig. 17.—Pulse volume of a subject who did not dilate during body heating. *A*, After thirty-six minutes body heating (two extremities immersed). *B*, After foot had been immersed for ten minutes in water of 42° C. Room temperature 21° C. Reduction of original tracings to two-thirds. For abbreviations, etc., consult legend to Fig. 2.

D. The Blood Flow in Sympathectomized Extremities.—Following the interruption of the sympathetic pathways the spontaneous fluctuations in pulse volume and digital volume, as well as the constrictor reflexes following various intrinsic and extrinsic stimuli, are no longer obtained (Fig. 18). Body heating fails to produce reflex dilatation, indicating that the body is no longer capable of mobilizing the peripheral blood flow for body temperature regulation. Conversely, interruption of the sympathetic reflex arc may be diagnosed from failure to evoke these responses.

Following ganglionectomy, the tone of the peripheral vessels is mainly determined by three factors: (1) the local metabolic requirements of the tissues (effect of metabolites), (2) the local stimuli reaching the vessel wall directly from the outside, without the mediation of the nervous system (cold, etc.), and (3) the effect of endogenous substances (acetylcholine, epinephrine, etc.) reaching the vessel wall via the blood stream. Therefore, the blood flow of the

Fig. 18.—Pulse volume following lumbar ganglionectomy. Note absence of changes in height of pulse and digital volume. *A*, Sympathectomy for ulcers ten years previously. (At signals: pinpricks). First left toe. Skin temperature 33° C. At arrow, accidental deep breath. *B*, Sympathectomy for Raynaud's phenomenon eight years previously. First left toe. Skin temperature 32° C. Note organic involvement. *C*, Sympathectomy for early thromboangiitis obliterans nine years previously. First right toe. Skin temperature 34° C. *D*, Sympathectomy for early thromboangiitis obliterans nine years previously. First right toe, elevated. Skin temperature 30° C. At signal, unexpected noise. Reduction of original tracings to two-thirds. For abbreviations, etc., consult legend to Fig. 2.

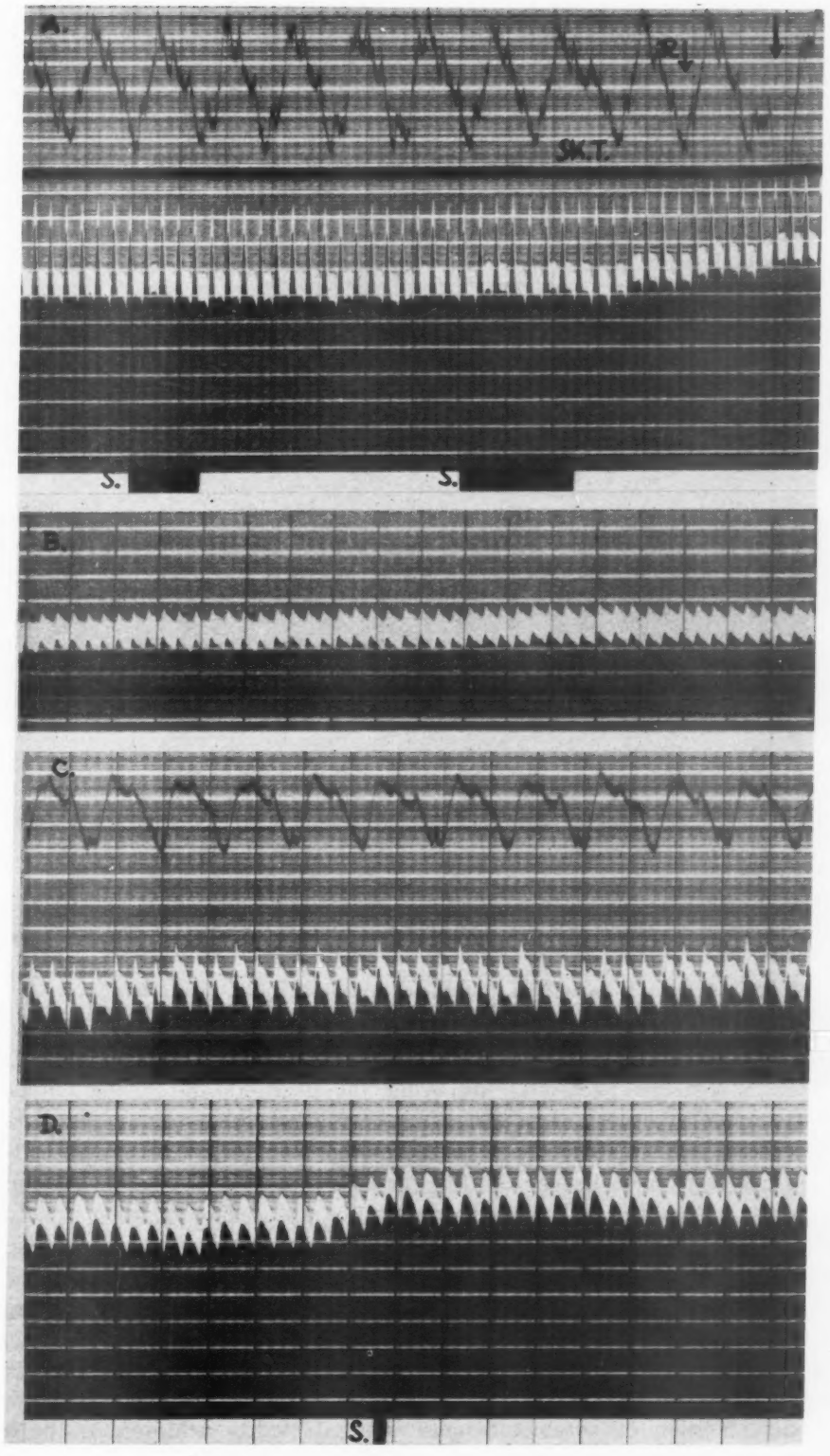

Fig. 18.—(*For legend see opposite page.*)

sympathectomized extremity may not be the same when tested on different occasions. If such influences are depressing in nature, the blood flow tends to return to its maximum as soon as such stimuli are removed. For this reason, during rest under ordinary laboratory conditions, the blood flow through the sympathectomized lower extremity was found to be at its maximum.

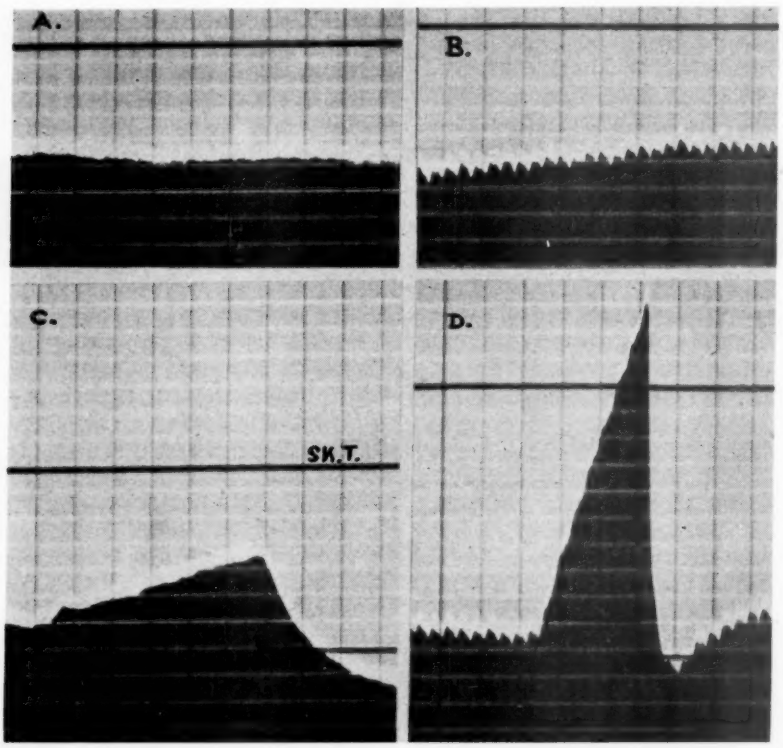

Fig. 19.—Subject with well-advanced thromboangiitis obliterans with superimposed arterial spasm (first right toe). *A*, Pulse volume during rest. Skin temperature 24.5° C. *B*, Pulse volume fully dilated. Skin temperature 32.5° C. *C*, Venous congestion test during rest. *D*, Venous congestion test fully dilated. Room temperature 23° C. Reduction of original tracings to two-thirds. For abbreviations, etc., consult legend to Fig. 2.

As is generally accepted, following the degeneration of the autonomic (postganglionic) nerves after ganglionectomy, there occurs an increased sensitivity of the isolated structure to circulating epinephrine. This hypersensitivity which has been made responsible for the early return of the vasomotor tone in the upper extremities following the removal of the stellate ganglion[15, 41, 47] does not enter the picture in this account, however, owing to the fact that ganglionectomy of the lower extremities does not remove the sympathetic ganglia supplying the sciatic nerve but interrupts their preganglionic fibers only. Degeneration of the sympathetic nerves to the foot therefore is not a feature of lumbar ganglionectomy and sensitization to epinephrine, which should theoretically be absent, is in fact minimal. Thus the aim of all ganglionectomies, namely permanent abolition of vasomotor tone, is more readily achieved in the lower

extremities. Thus we found in 29 patients in whom 51 lumbar ganglionectomies had been performed from one to eleven years previous to the last examination that the blood flow was still at its maximum and that there was no return of vasomotor tone as judged by the height of the pulse volume and the rate of the blood flow. There was no increase in blood flow following body heating. Obviously, even in the subject with sympathectomy of longest duration (Fig. 18, *A*) regeneration of the sympathetic fibers had not occurred, which bears emphasis in the light of the work of various authors.[25, 43, 47]

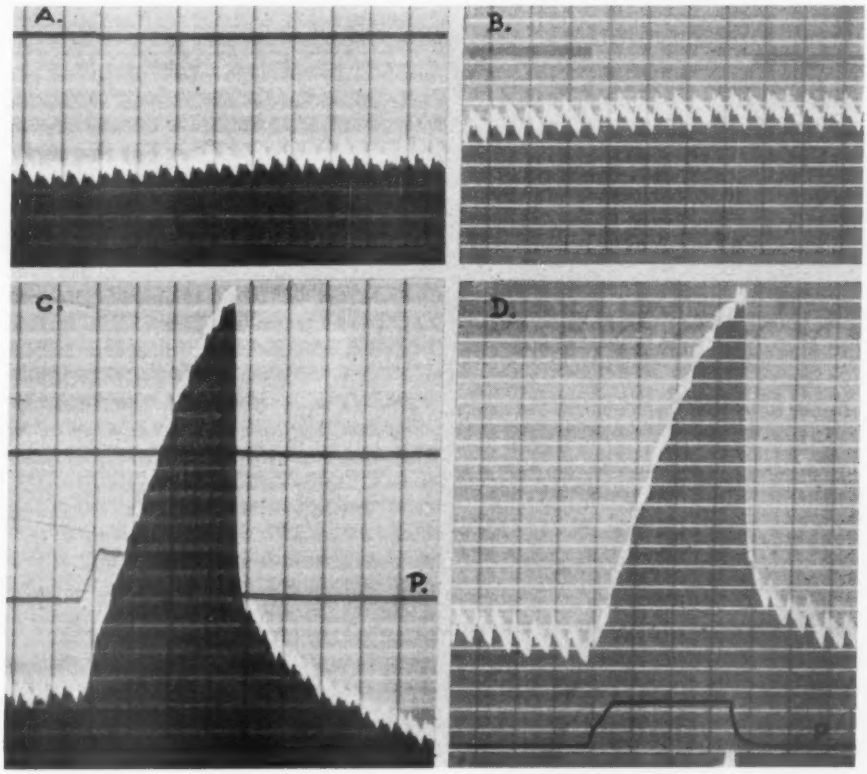

Fig. 20.—Same subject as Fig. 19 (first right toe). *A*, fourteen days after lumbar sympathectomy. Skin temperature 32° C. *B*, Thirteen months after sympathectomy. Skin temperature 34° C. *C*, Venous congestion (fourteen days after sympathectomy). *D*, Venous congestion (thirteen months after sympathectomy). Reduction of original tracings to two-thirds. Room temperature 22° C. For abbreviations, etc., consult legend to Fig. 2.

The indications for sympathectomy in peripheral vascular diseases depend upon the demonstration of a significant degree of vasoconstriction. The latter can be determined exactly by digital plethysmography and the amount of relaxation which can be expected to result from sympathectomy can be predicted exactly. Fig. 19 was obtained from a subject with histologically proved thromboangiitis obliterans, demonstrating the point in question. No pulse volume was registrable during ordinary laboratory conditions (Fig. 19, *A*), and the rate of blood flow amounted to 2.2 c.c. for 100 c.c. of tissue per minute (Fig. 19, *C*). Body heating, however, greatly increased the blood flow. The pulse volume rose

to 0.005 c.c. (Fig. 19, *B*), the skin temperature to 31° C., and the rate of blood flow increased exactly ten times to 22.5 c.c. (Fig. 19, *D*). Two weeks after the ganglionectomy the values for both pulse volume and rate of blood flow were at the preoperative vasodilatation level (Fig. 20, *A* and *C*) and when tested one year after the operation they had even increased slightly (Fig. 20, *B* and *D*).

In our cases where lumbar sympathectomies were performed for other than vascular diseases (e.g., ulcus cruris) both pulse volume and rate of blood flow reached and remained at the normal vasodilatation level (Fig. 18, *A*).

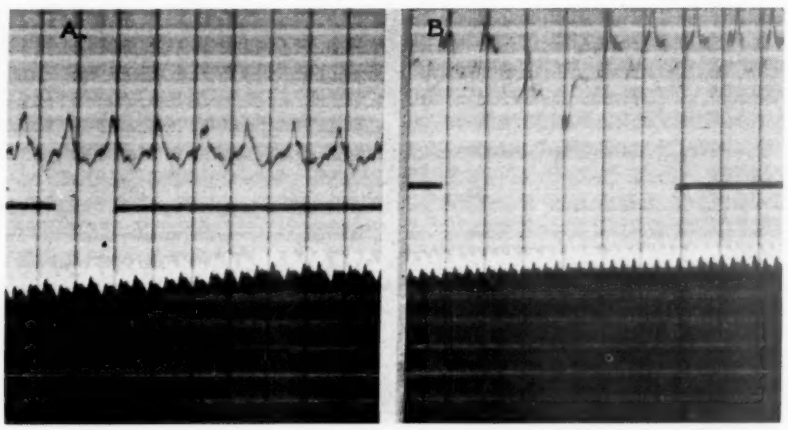

Fig. 21.—Decrease of pulse volume in sympathectomized extremity on body heating (same subject as Fig. 20, fourteen days after sympathectomy). *A*, Before body heating. *B*, After thirty minutes body heating. Reduction of original tracings to two-thirds.

In order to avoid confusion, all I have mentioned so far is that body heating does not increase the pulse volume and rate of blood flow in the completely sympathectomized extremity. The fact, however, is that both pulse volume and rate of blood flow decrease, often notably, with body heating (Fig. 21). The opposite may be observed following body cooling when pulse volume and rate of blood flow reach higher values. This decrease in blood flow following body heating has been explained as follows: At the outset it must be assumed that the blood is shunted away from the sympathectomized extremity. Then, since body heating causes a release of the vasomotor tone in the remaining normally innervated extremities, it follows that their vessels will offer less resistance to the blood flow as dilatation takes place, as contrasted with the vessels of the sympathectomized limb (the vascular tone of which remains uninfluenced by body heating and which consequently presents itself as being increased); and the blood flow, choosing the path of least resistance, will therefore be diverted from the sympathectomized extremity to the unsympathectomized one.

A similar phenomenon, occurring for the same reason, was observed in limbs showing marked signs of inflammation. Inflammation results in paralysis of vasoconstrictor tone, and body heating often does not raise skin temperature but decreases it in the inflamed limb.

These findings are not only of academic interest, but important in the management of peripheral vascular diseases in general and in sympathectomized limbs in particular. Methods normally known to cause increase in blood flow by reflex mechanisms may actually be contraindicated in the treatment of lesions in sympathectomized and inflamed extremities, since they may have the opposite of the desired effect.

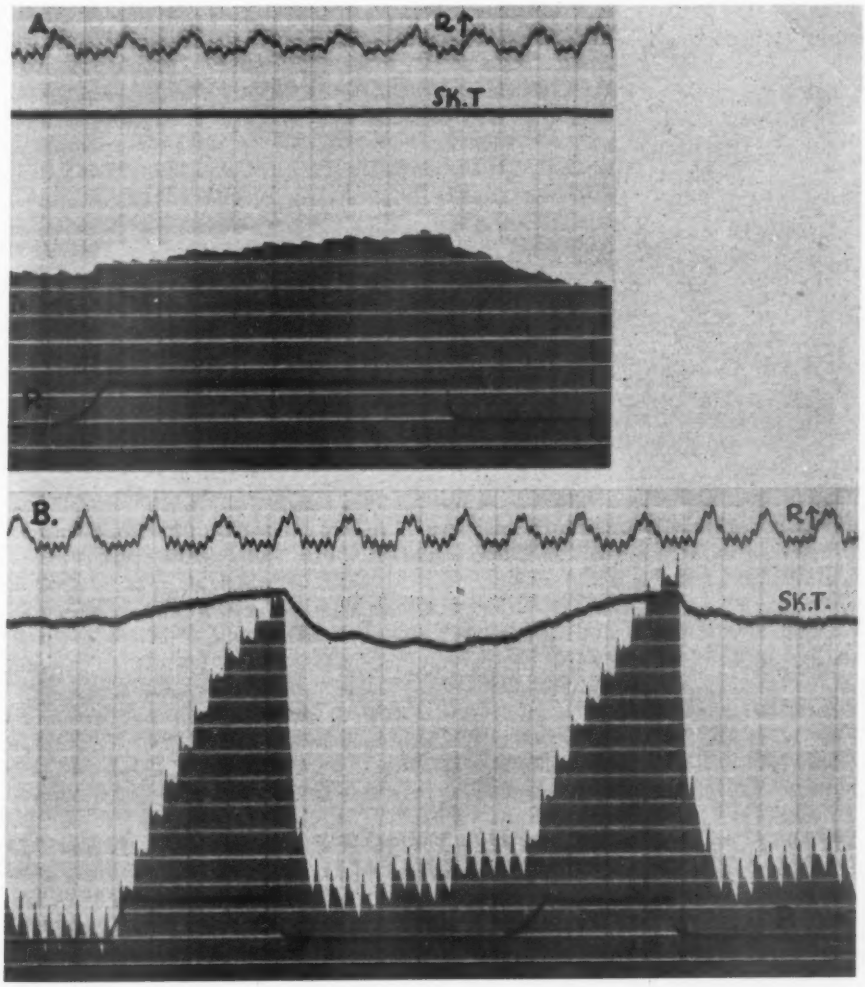

Fig. 22.—Case 1: Subject with Raynaud's phenomenon (first right toe). *A*, Venous congestion test during rest. Skin temperature 22° C. *B*, Venous congestion test during full dilatation. Skin temperature ±34° C. Reduction of original tracings to two-thirds. For abbreviations, etc., consult legend to Fig. 2.

E. The Blood Flow in Peripheral Vascular Diseases.—It is outside the scope of this paper to deal with any of the vascular disorders in detail. We merely propose to demonstrate how our method may help in elucidating some of the more important clinical problems. Whenever a patient with symptoms

referable to the peripheral circulatory system is observed, three questions arise: (1) Is there an organic or a functional interference of the blood flow? (2) If organic, how advanced is the occlusion and to what extent are the vessels still capable of dilatation? (3) In cases where the main vessels are completely obliterated, how well has the collateral circulation been developed? It is true that skin temperature measurements will furnish some information, but it is the knowledge of the exact amount of blood flowing through the part which is so particularly helpful in organic occlusions, especially when it comes to the determination of the collateral circulation.

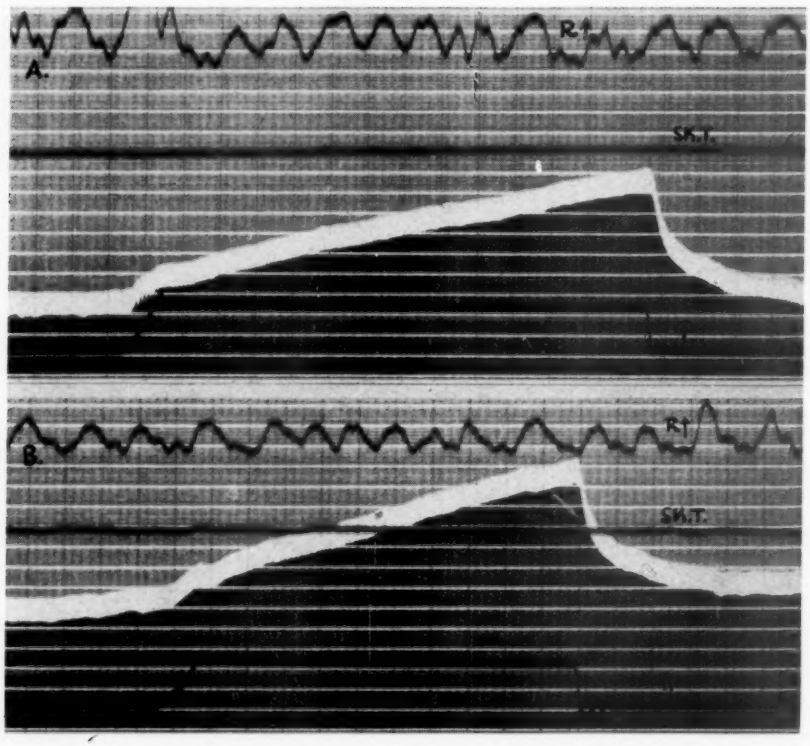

Fig. 23.—Case 2: Complete organic occlusion (first left toe). *A*, Venous congestion during rest. Skin temperature 28.7° C. *B*, Fully dilated. Skin temperature 29.3° C. Reduction of original tracings to two-thirds. For abbreviations, etc., consult legend to Fig. 2.

In Figs. 22, 23, and 24, three patients are presented, in all of whom there is a poor blood circulation during rest, as judged by the pulse volume and the rate of blood flow. However, in the first case, body heating results in a relatively normal response (Fig. 22). All values increase rapidly almost to within the normal limits. The diminished blood flow was therefore due to a high vasomotor tone only, there being hardly any organic interference demonstrable. The second case is exactly the opposite—no rise was noted either in pulse volume or in the venous congestion test with body heating (Fig. 23). The rate of blood flow remained almost the same. This is therefore a case of complete arterial occlusion. In the third case, as in the second, hardly any rise in pulse

volume was registered on body heating, which means that the main arteries must have been occluded. However, there was a marked increase in the rate of blood flow, which rose from 4.5 to 25 c.c. (Fig. 24). Obviously, it was the small collaterals in which the blood flow did not pulsate which dilated with body heating in this case. The venous congestion test, therefore, is capable of furnishing us with an exact measurement of the collateral circulation. A typical example of a case showing moderate organic occlusion associated with considerable spasm has already been demonstrated (Fig. 19).

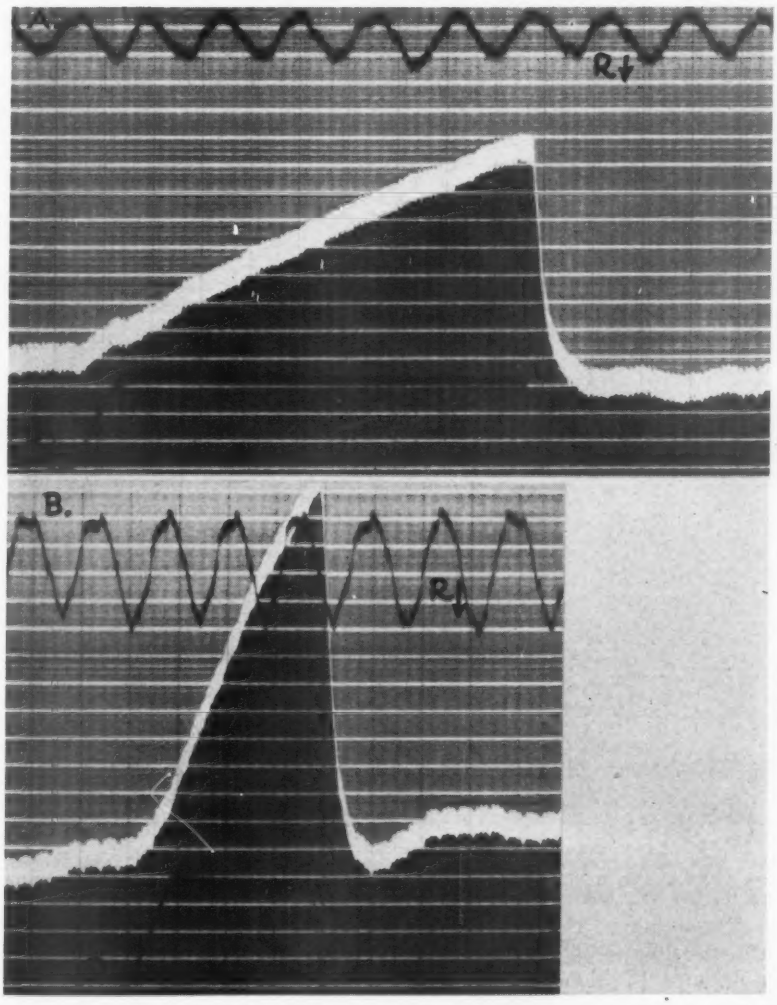

Fig. 24.—Case 3: Organic occlusion with well-developed collateral circulation (first left toe) (thromboangiitis obliterans). *A*, During rest. Skin temperature 22.5° C. *B*, Fully dilated. Skin temperature 28° C. Note the increase in venous congestion test out of proportion to minimal rise in pulse volume. Reduction of original tracings to two-thirds. For abbreviations, etc., consult legend to Fig. 2.

The degree to which the blood flow has to be diminished to cause death of tissue is surprising: reduction of the blood flow by 60 per cent has been found in many arteriosclerotic subjects who show no clinical manifestations of im-

paired peripheral circulation. This bears out the point made earlier that the blood flow through the digits serves other functions in addition to tissue metabolism. Permanent diminution of the blood flow to as little as 3 to 5 c.c. per minute for 100 c.c. of tissue occurred in some patients without causing gangrene.

According to these findings a rate of blood flow of 3 c.c. is all that is permanently needed for local tissue metabolism of the skin. This figure is somewhat higher than that computed by Burton.[8] It is important to realize that in such cases gangrene may be precipitated not by deficient blood flow per se, but

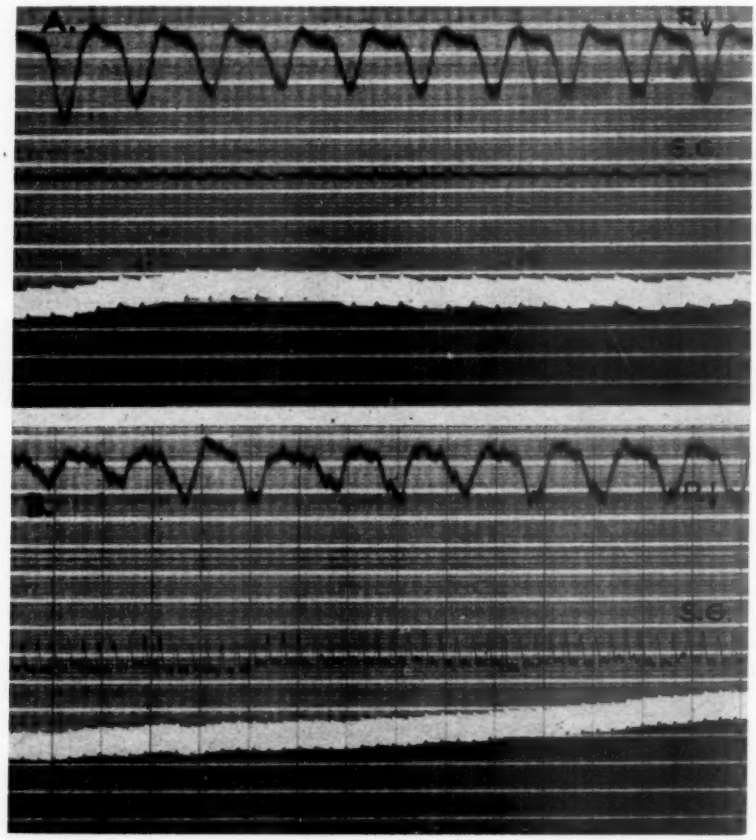

Fig. 25.—Plethysmogram and sphymogram in two cases of diminished peripheral (ultimate) blood flow, but showing differences in penultimate circulation. *A*, first left toe. Skin temperature 19.5° C. *B*, first right toe. Skin temperature 21° C. Reduction of original tracings to two-thirds. For abbreviations, etc., consult legend to Fig. 2.

by a precipitating factor (such as heat and inflammation) suddenly demanding a higher amount of blood flow which in the organically occluded vessel is not forthcoming and which results in tissue death. It is not generally realized what degree of obstruction is required to produce a known reduction in blood flow. According to Poiseuille's law, the rate of blood flow changes as the fourth power of the radius of the vessel lumen. Diminution of the diameter of the lumen by one-half will therefore cause a drop in the rate of blood flow to one-sixteenth of that particular vessel.

Information as to the site of a peripheral obstruction of the blood flow may be obtained by recording simultaneously both the plethysmogram of a toe and the sphygmogram of the arteria dorsalis pedis. In both patients illustrated in Fig. 25 there was marked diminution of the peripheral blood flow, the pulse volume being only 0.002 cubic centimeter. In the first case, the excursions of the arteria dorsalis pedis were markedly diminished as well, demonstrating involvement of the whole arterial tree. Good excursions of the dorsalis pedis artery in the other case, however, placed the site of the interference at the arterioles, the penultimate circulation being hardly impaired.

DISCUSSION

Three values are furnished by the digital plethysmogram: (1) the pulse volume, (2) the digital volume, and (3) the rate of blood flow (by means of the venous congestion test). By recording simultaneously skin temperature and the excursions of one of the peripheral arteries a detailed analysis of the peripheral blood flow and vasomotor activity becomes possible. Of these, the height of the pulse volume is the most delicate indicator of both vasomotor activity and structural changes of the arteries. Its normal range varied between 0.002 c.c. during full constriction and 0.045 c.c. with full dilatation. The lowest value recorded during full dilatation in normal subjects was 0.02 c.c. and is referred to as the minimum vasodilatation level. These values compare very well with the height of the pulse volume previously recorded in the fingers.[20, 21, 23] Failure of the pulse volume to reach the minimum vasodilatation level has yet to be accounted for.

While the pulse volume is intimately correlated with the actual rate of blood flow, and can therefore be used as an index for detailed analysis of the latter, the arterial inflow can be measured exactly by the venous congestion test. Its range varied between 1 c.c. per minute for 100 c.c. of tissue during full constriction and 90 c.c. per minute during full dilatation. The latter value is about four times higher than that calculated by Kunkel and Stead[30] for the whole foot, while the lower range is about the same, suggesting that it constitutes the minimal requirement for tissue metabolism. In the upper extremities similar relations exist, the blood flow through the hand being about one-fourth of that through the fingers.[23]

The possibility exists that such a wide range in blood flow under the control of the autonomic nervous system is part of the body's mechanism for temperature regulation. The skin acts, as Sheard puts it, as an enormous dam with many gateways placed across the stream of internal heat, which can be opened and closed as occasion demands. Indeed, Winslow, Herrington, and Gagge[49] found that, by adjustment of the peripheral circulation, the effective thermal conductivity of the tissue may be modified over a fivefold to sixfold range. It is by means of the sympathetic tone that the blood flow through the extremities is set to the level prescribed by the demands of thermoregulation. Consequently, the tone of the vessels of the fingers under ordinary circumstances (room temperature, 20° to 23° C.) is about midway between full dilatation and full constriction, allowing the necessary adjustment.[23] In the toes, however, the vaso-

motor tone is, as a rule, considerably higher; and the blood flow, being near the lower limit, is not mobilized for thermoregulation. However, the picture changes and the vasomotor tone of the toe vessels decreases to take part in thermoregulation the moment the capacity of the blood flow through the fingers has been fully utilized. Dissipation of heat is initiated by the hands and forearms and continued by the feet and legs. These findings agree well with the observations of Roth, Horton, and Sheard[39] that the skin temperature of the toes noticeably exceeds room temperature only when that of the fingers fluctuates between 33° and 35° C.

Once the high vasomotor tone of the toe vessels has been overcome, spontaneous changes in the blood flow through the toes occur just as they were recorded in the fingers. They are best studied with the limb elevated when changes both in pulse volume and in toe volume assume very marked proportions. They are less prominent when the limbs are dependent. Abramson and Katzenstein[2] reported that spontaneous fluctuations are characteristic for the hands but that they are absent or insignificant in the feet. Our investigations make it more than likely that the reason for his apparent difference between the upper and lower extremities is due to differences in posture and is not the result of differences in vasomotor activity. In Abramson and Katzenstein's tests the foot was obviously dependent.* There can be no doubt that spontaneous changes in blood flow are typical for both fingers and toes—they can be readily recorded under identical conditions which includes identical vasomotor tone and identical hemostatic conditions. Since they are more prominent in the elevated extremity we conclude that they are arterial rather than venous in origin, in contrast to the view of Abramson.

Ever since Brown-Sequard[7] called attention to the clinical importance of differentiating arterial spasm from arterial occlusion, tests measuring the degree of both have become an essential requirement in the study of peripheral vascular diseases. Of these the immersion test introduced by Gibbon and Landis[18, 32] has proved a very efficient and unobjectionable method of producing reflex dilatation. Pickering and Hess,[37] however, in one apparently healthy subject, failed to obtain relaxation of the vasomotor tone of the feet with immersion of the hands and concluded that warming of the body removes only part of the constrictor tone of the feet, "the remainder being more or less permanent unless the sympathetic fibres are blocked." The studies in our series did not corroborate this. Whenever body heating released vasomotor tone complete dilatation was produced. The height of the pulse volume and rate of blood flow obtained after body heating corresponded well with the values obtained following direct application of heat or during paravertebral block.

Body heating is a most effective method of producing complete reflex dilatation. However, similarly to the case already reported by Pickering and Hess, in two of our own cases body heating failed to release vasomotor tone. Therefore, in subjects who do not respond to body heating, but in whom there is obviously incomplete organic occlusions on clinical examination, we produce

*No mention of the position is made.

maximal dilatation by following body heating with the local application of heat. The question of whether we are dealing with an organic or a functional state is then easily answered. This simple method can be used with great advantage in conjunction with plethysmography, but it is obviously useless if the circulation is assessed by means of skin temperature measurements and when more complicated methods like paravertebral block or spinal anesthesia have to be resorted to to assure release of vasomotor tone.

Gibbon and Landis[18, 32] have already recognized that it is the increase in blood temperature due to the return of heated blood from the immersed extremity acting upon the thermosensitive centers in the hypothalamus which initiates general reflex vasodilatation. Pickering[36] estimated that a rise of 0.01° to 0.04° C. is sufficient to produce this effect. Soon afterward Carmichael and his coworkers[44] pointed out that it is the gradient or steepness of the rise rather than the actual temperature of the blood itself which initiates relaxation. Thus, the rate of blood flow through the immersed extremity becomes an important factor in securing vasodilatation. With organic occlusion of the arteries in the immersed extremity, the amount of heated blood returned will be insufficient to produce the necessary gradient and dilatation may be incomplete or absent, even if the vessels of the tested extremity are absolutely normal. This is not a theoretical possibility but occurs in practice. Indeed, in the disorders seen in the majority of patients, such as thromboangiitis obliterans and arteriosclerosis, involvement of all extremities to varying degrees is the rule. Thus, failure of the immersion method to produce reflex dilatation may not mean necessarily organic occlusion of the limb tested, but may mean organic occlusion of the immersed extremity, nothing being revealed about the vessels in the extremity under examination. Obviously, this source of error is not inherent in methods producing dilatation by interrupting the sympathetic pathways or by direct application of heat.

Gibbon and Landis[18, 32] were of the opinion that a rise in skin temperature to 32° C. within thirty to thirty-five minutes "definitely excludes the possibility of obliterative structural disease of the arteries," a view which now is generally held. Accordingly, Jahsman and Durham,[27] discussing the early recognition of arterial disease, state that "such a response excludes the possibility of obliterating structural disease of the arteries." Our investigations do not support their statements. Indeed, the blood flow measured plethysmographically may be diminished by as much as 60 per cent before significant alterations in the response of the skin temperature to body warming occur! A normal skin temperature after body heating, then, is no criterion as to the efficiency of the arterial circulation. The skin temperature response to body heating is not impaired in early organic involvement of the arteries, whereas the pulse volume in plethysmographic tracings is already markedly decreased. Realization of this fact becomes of paramount importance today when one is called upon to examine apparently healthy young men of our Armed Forces for what appear to be minor complaints but in whom the question of vascular disease arises. By waiting for the skin temperature to indicate arterial deficiency all the early cases of disease will be missed and in many of them a good prognosis vitiated.

Plethysmographic investigations therefore become almost essential since it may not be possible without them to answer the question of early structural changes.

The following sentence from Freeman and his co-workers' recent article[34] represents the typical opinion prevailing today as to the significance of skin temperature readings: "With a cool room temperature (20° C.) a rise in skin temperature to 31° C. means that the flow of blood is equal to that of a normal person with full vasodilatation. This level is reached in a limb with no arterial occlusion or with arterial occlusion which has been completely compensated for by collateral circulation." This statement admits that skin temperature readings do not indicate whether there is a normal blood flow or an arterial occlusion which has been compensated for by the development of a collateral circulation. The distinction between the two, one being normal, the other an indication of a serious pathologic event, is of considerable importance for the individual concerned and can by no means always be decided on clinical evidence. Neither does the fact that the arterial occlusion has been compensated for by a collateral circulation indicate that the underlying disorder has been arrested. By assessing the degree of both arterial occlusion and collateral circulation in such a case, plethysmographic investigations will assist us greatly in arriving at the correct diagnosis and prognosis.

Kramer[29] in his monograph on peripheral vascular diseases states that the usefulness of the plethysmograph is "more along the lines of investigation work and physiological research." I hope to have made it clear that the method developed by me lends itself at least as well to routine clinical examinations and furnishes information which cannot be obtained by any other method. The time has arrived when its wider use in clinics can be advocated. Its essentiality in recognizing early structural changes has been stressed. In differentiating occlusive from spastic vascular disease it has the advantage of supplying exact figures for the rate of blood flow, permitting exact estimation of the relative degree of each in a mixed case. In advanced cases the evaluation of the peripheral circulation revolves round the presence or absence of an adequate collateral circulation which can readily be determined by the venous congestion test. Such information is of prime importance because the principles on which the treatment of these groups must rest differ radically.

SUMMARY AND CONCLUSIONS

A plethysmographic method for measurement of the blood flow through the skin of the toes is described. The method is sensitive enough to register the blood flow through even a small toe in all its detail. The plethysmogram obtained furnishes three values: the pulse volume, changes in the digital volume, and, by means of the venous congestion test, the rate of blood flow. Of these, the height of the pulse volume was found to be an exquisite indicator of both organic occlusion and vasomotor tone. It varied normally between 0.002 c.c. during constriction and 0.045 c.c. during full dilatation.

Under ordinary laboratory conditions the vasomotor tone in the lower extremities is much higher than that of the upper ones, their blood flow not being mobilized for body temperature regulation like that of the hands. Dissipation

of heat is primarily effected by the hands and forearms, and only when their capacity has been fully exhausted does the vasomotor tone in the toe vessels decrease and then their blood flow is used for body temperature regulation. Data furnished suggest that this mechanism is the result of man's assumption of the upright posture. Spontaneous changes in blood flow are less prominent in the lower extremities on account of the high vasomotor tone, but they become equally marked, as in the upper extremities, once identical conditions prevail.

The rate of blood flow varied normally between 1 c.c. during full constriction and 90 c.c. per minute for 100 c.c. of tissue during full dilatation.

The effect of body heating as obtained by immersion of an independent extremity was studied. It is the gradient of the rise in blood temperature effect by the heated blood returned which initiates dilatation. Thus, a normal blood flow through the *immersed* extremity becomes very important.

It was found that the blood flow need not be normal if the skin temperature reaches 32° within thirty minutes (the "normal vasodilatation level") but may be markedly diminished as judged by the results of plethysmographic investigations. Plethysmography is therefore essential for detecting early structural lesions. The histologic appearance in such a case is shown, proving the point in question.

Once the release of the vasomotor tone is initiated, dilatation is maximal with body heating. However, two cases are cited in which release of vasomotor tone did not occur with body heating. Local application of heat in these cases easily demonstrated the patency of the vessels.

The indication for sympathectomy is discussed. In our cases following lumbar sympathectomy there was no return of vasomotor tone in the toes, and no regeneration could be demonstrated. In the sympathectomized extremity body heating decreases the pulse volume, by diverting blood from the sympathectomized extremity to the normal ones. Its clinical importance was stressed.

It is shown that the study of peripheral vascular disease is greatly assisted by plethysmographic investigations. Exact information becomes available as to the degree of occlusion, the degree of spasm, and the degree of the collateral circulation. By recording simultaneously excursions of one of the palpable arteries, the skin temperature, and the plethysmogram, detailed analysis of the peripheral blood flow becomes possible.

It is with pleasure that I acknowledge my indebtedness to Professor C. F. M. Saint for the interest he has taken in this work and for his helpful criticism.

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REFERENCES

1. Abramson, D. L., and Ferris, E. B.: Am. Heart J. 19: 541, 1940.
2. Abramson, D. I., and Katzenstein, K. H.: Am. Heart J. 21: 191, 1941.
3. Abramson, D. I., Zazeela, H., and Marrus, J.: Am. Heart J. 17: 194, 1939.
4. Abramson, D. I., Zazeela, H., and Marrus, J.: Am. Heart J. 17: 206, 1939.
5. Allen, E. V., and Crisler, G. R.: J. Clin. Investigation 16: 649, 1937.

6. Bolton, B., Carmichael, E. A., and Sturup, G.: J. Physiol. 86: 83, 1936.
7. Brown-Sequard, C. E.: Course of Lectures on the Physiology and Pathology of the Central Nervous System. Delivered at the Royal College of Surgeons of England in May, 1858. Philadelphia, 1873, p. 148.
8. Burton, A. C.: Am. J. Physiol. 127: 437, 1939.
9. Capps, R. B.: J. Clin. Investigation 15: 229, 1936.
10. Donegan, J. F.: J. Physiol. 55: 226, 1921.
11. Doupe, J., Robertson, J. S., and Carmichael, E. A.: Brain 60: 281, 1937.
12. Ferris, E. B., and Abramson, D. I.: Am. Heart J. 19: 233, 1940.
13. Ferris, E. B., and Abramson, D. I.: Publication No. 13 American Association for the Advancement of Science, p. 314.
14. Freeman, N. E.: Am. J. Physiol. 113: 384, 1935.
15. Freeman, N. E., Smithwick, R. H., and White, J. C.: Am. J. Physiol. 107: 529, 1934.
16. Friedlander, M., Silbert, S., Bierman, W., and Laskey, N.: Proc. Soc. Exper. Biol. & Med. 38: 150, 1938.
17. Fulton, J. F.: Physiology of the Nervous System, London, 1938, Oxford University Press.
18. Gibbon, J. H., and Landis, E. M.: J. Clin. Investigation 11: 1019, 1932.
19. Goetz, R. H.: Klin. Wchnschr. 44: 1717, 1933.
20. Goetz, R. H.: Pflüger's Arch. f. d. ges. Physiol. 235: 271, 1935.
21. Goetz, R. H.: Brit. J. Surg. 27: 506, 1939.
22. Goetz, R. H.: Clin. Proc. 1: 190, 1942.
23. Goetz, R. H.: South African J. M. Sc. 8: 65, 1943.
24. Grant, R. T., and Pearson, R. S.: Clin. Sc. 3: 119, 1938.
25. Haimovici, H., and Hodes, R.: Am. J. Physiol. 128: 463, 1940.
26. Horton, B. T., Roth, G. M., and Adson, A. W.: Proc. Staff Meet., Mayo Clin. 11: 433, 1936.
27. Jahsman, W. E., and Durham, R. H.: Ann. Int. Med. 18: 164, 1943.
28. Kolin, A.: Proc. Soc. Exper. Biol. & Med. 42: 85, 1939.
29. Kramer, D. W.: Manual of Peripheral Vascular Disorders, Philadelphia, 1940, P. Blakiston's Son & Co.
30. Kunkel, P., and Stead, E. A.: J. Clin. Investigation 17: 715, 1938.
31. Kunkel, P., Stead, E. A., and Weiss, S.: J. Clin. Investigation 18: 225, 1939.
32. Landis, E. M., and Gibbon, J. H.: Arch. Int. Med. 52: 785, 1933.
33. Lewis, T.: The Blood Vessels of the Human Skin and Their Responses, London, 1927, Shaw & Sons, Ltd., p. 34.
34. Montgomery, H., Naide, M., and Freeman, N. E.: Am. Heart J. 21: 780, 1941.
35. Peters, G.: Pflüger's Arch. f. d. ges. Physiol. 241: 201, 1938.
36. Pickering, G. W.: Heart 16: 115, 1932.
37. Pickering, G. W., and Hess, W.: Clin. Sc. 1: 213, 1933.
38. Rein, H.: Ergebn. d. Physiol. 32: 28, 1931.
39. Roth, G. M., Horton, B. T., and Sheard, C.: Am. J. Physiol. 128: 782, 1940.
40. Silbert, S.: J. Mt. Sinai Hosp. 5: 128, 1938.
41. Smithwick, R. H., Freeman, N. E., and White, J. C.: Arch. Surg. 29: 759, 1934.
42. Stead, E. A., and Kunkel, P.: J. Clin. Investigation 17: 711, 1938.
43. de Takats, G.: Arch. Int. Med. 60: 990, 1937.
44. Uprus, V., Gaylor, J. B., and Carmichael, E. A.: Clin. Sc. 2: 301, 1936.
45. Uprus, V., Gaylor, J. B., Williams, D. J., and Carmichael, E. A.: Brain 58: 448, 1935.
46. Warren, J. V., Walter, C. W., Romano, J., and Stead, E. A.: J. Clin. Investigation 21: 665, 1942.
47. White, J. C., and Smithwick, R. H.: The Autonomic Nervous System, ed. 2, London, 1942, Henry Kimpton.
48. Williams, M. M. D., Horton, B. T., and Sheard, C.: Proc. Staff Meet., Mayo Clin. 14: 668, 1939.
49. Winslow, C.-E. A., Herrington, L. P., and Gagge, A. P.: Am. J. Physiol. 120: 1937.
50. Wright, G. W., and Phelps, K.: J. Clin. Investigation 19: 273, 1940.

ELECTROCARDIOGRAPHIC CHANGES IN CASES OF INFECTIOUS HEPATITIS

Study of Eleven Cases Occurring in an Epidemic

Helmut Dehn, M.D., Harold Feil, M.D., and Robert E. Rinderknecht, M.D.
Cleveland, Ohio

THE sinus bradycardia observed in cases of jaundice is well known, but we have been unable to find any report of clinical electrocardiographic observations in the literature. Several experimental studies in animals have been made in order to determine the mechanism of the bradycardia and of the lowering of the blood pressure. A recent epidemic of infectious jaundice gave us an opportunity to study the electrocardiograms of this disease; eleven cases were studied during the height of the jaundice and after recovery.

REPORT OF CASES IN EPIDEMIC

In all, there were twenty-four cases of infectious hepatitis. The patients were all medical students and were in normal physical condition previously.

In none of the subjects had there been vaccination for yellow fever or other innoculation immediately preceding the outbreak. All the patients were members of one fraternity and ate at the same table. The subjects were all febrile, the temperature in some cases rising to 40° C. and above. All patients survived, and there were no sequelae. Other than the bradycardia, there were no cardiac symptoms. The Wassermann and microprecipitation tests were negative in all instances. The cephalin flocculation test was positive in all cases. The agglutination test for *Leptospira icterohaemorrhagiae* was negative in all cases. The clinical data are summarized in Table I.

Table I. Clinical Features

Case	Temperature (°C.)		Blood Pressure	Leucocytes (per cu. mm.)		Albumin in Urine	Icterus Index		Liver*
	Admission	Highest		Admission	Highest		Admission	Highest	
1	38.6	38.6	120/80	5,400	8,600	0	7	15	+T
2	37.6	38.0	120/70	5,750	6,750	tr	24	24	+T
3	39.6	39.6	120/70	5,600	8,200	tr	20	20	+T
4	40.2	40.2	130/80	2,700	5,650	0	6	55	+T
5	40.1	40.1	145/70	5,850	8,550	0	11	26	+T
6	39.3	39.9	130/60	5,800	8,800	S.P.T.	16	24	T
7	37.2	37.9	120/75	5,950	6,100	0	14	19	+T
8	37.9	38.4	120/80	6,350	9,050	S.T.		35	T
9	38.4	39.3	130/80	5,050	6,000	0	7	11	+T
10	39.6	40.5	100/60	5,200	5,700	S.P.T.	17	22	+
11	37.5	37.5	Not recorded	5,200	5,200	0	45	45	+T

*+, palpable; *T*, tenderness; *tr*, trace; *S.P.T.*, slightest possible trace.

From the Department of Medicine of Western Reserve University School of Medicine and from Lakeside Hospital, Cleveland, Ohio.
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TABLE II. COMPARISON OF T-WAVE CHANGES WITH DEGREE OF JAUNDICE

CASE	HEART RATE PER MINUTE		T WAVE (HEIGHT IN MM.)			ICTERUS INDEX
	ILLNESS	RECOVERY	ILLNESS		RECOVERY	
1	70	73	Lead I	2.0	3.5	15
			Lead II	3.0	5.5	
			Lead III	1.5	1.5	
2	68	84	Lead I	2.5	3.5	24
			Lead II	2.5	4.5	
			Lead III	1.0	1.5	
3	61	93	Lead I	1.75	2.5	20
			Lead II	3.5	4.0	
			Lead III	1.5	2.0	
4	66	63	Lead I	2.5	3.5	55
			Lead II	2.0	3.5	
			Lead III	−1.0	+−	
5	66	100	Lead I	2.0	2.0	26
			Lead II	2.5	3.0	
			Lead III	1.0	1.0	
6	52	91	Lead I	0.75	1.5	24
			Lead II	0.5	1.0	
			Lead III	+−	+−	
7	56	73	Lead I	1.75	2.5	19
			Lead II	0.5	1.0	
			Lead III	−1.0	−1.0	
8	80	75	Lead I	2.0	4.0	35
			Lead II	2.5	5.5	
			Lead III	1.0	1.5	
9	55	76	Lead I	3.0	4.0	11
			Lead II	5.0	4.0	
			Lead III	1.5	1.0	
10	102	48	Lead I	1.5	2.5	22
			Lead II	2.5	4.0	
			Lead III	1.5	1.5	
11	64	59	Lead I	2.0	2.0	45
			Lead II	1.5	2.0	
			Lead III	−0.5	1.0	

ELECTROCARDIOGRAPHIC FINDINGS

Electrocardiograms were taken in all eleven cases (Leads I, II, and III) on admission and after recovery. Table II is a summary of the heart rate, the height of the T wave, and the icterus index.

On comparing the T-wave changes with the icterus index, no correlation was seen. Likewise the temperature had little influence on the heart rate—some of the higher rates were found in the patients with lower temperatures and with high icterus indices, as noted in Table I.

In all instances, normal mechanism was present and, with it, sinus arrhythmia. In eight of the cases there was a moderate bradycardia during the height of the disease, and in two cases the heart rate was slightly higher than after convalescence. In one instance there was no change in heart rate.

TABLE III. Q-T INTERVAL DURING JAUNDICE AND AFTER RECOVERY

CASE	HEART RATE		CYCLE LENGTH		K (Q-T = K $\sqrt{VC}$)	
	JAUNDICED	RECOVERY	JAUNDICED	RECOVERY	JAUNDICED	RECOVERY
1	70	65	0.86	0.92	0.389	0.376
2	68	75	0.88	0.80	0.384	0.369
3	61	67	0.98	0.90	0.390	0.40
4	66	80	0.91	0.75	0.379	0.392
5	66	72	0.91	0.83	0.379	0.362
6	52	69	1.15	0.87	0.391	0.375
7	56	68	1.07	0.88	0.396	0.395
8	80	84	0.75	0.71	0.393	0.392
9	55	65	1.09	0.92	0.383	0.385
10	102	65	0.59	0.92	0.391	0.376
11	64	75	0.94	0.80	0.392	0.381

TABLE IV. EFFECT OF EXERCISE

CASE	AT REST			AFTER EXERCISE (HOPS)		
	HEART RATE	T WAVES (MV)		HEART RATE	T WAVES (MV)	
1	65	Lead I	0.35	86	Lead I	0.25
		Lead II	0.50		Lead II	0.35
		Lead III	0.10		Lead III	0.10
2	75	Lead I	0.35	96	Lead I	0.35
		Lead II	0.45		Lead II	0.40
		Lead III	0.15		Lead III	0.10
3	67	Lead I	0.20	82	Lead I	0.15
		Lead II	0.35		Lead II	0.30
		Lead III	0.15		Lead III	0.10
4	80	Lead I	0.30	113	Lead I	0.15
		Lead II	0.25		Lead II	0.15
		Lead III	−0.10		Lead III	−0.10
5	72	Lead I	0.20	84	Lead I	0.15
		Lead II	0.30		Lead II	0.25
		Lead III	0.10		Lead III	0.10
6	69	Lead I	0.10	84	Lead I	0.10
		Lead II	0.10		Lead II	0.10
		Lead III	−0.05		Lead III	−0.05
7	68	Lead I	0.25	88	Lead I	0.15
		Lead II	0.10		Lead II	0.15
		Lead III	−0.10		Lead III	−0.05
8	84	Lead I	0.40	103	Lead I	0.25
		Lead II	0.55		Lead II	0.40
		Lead III	0.15		Lead III	0.15
9	65	Lead I	0.40	78	Lead I	0.40
		Lead II	0.40		Lead II	0.45
		Lead III	0.10		Lead III	0.15
10	65	Lead I	0.25	107	Lead I	0.15
		Lead II	0.40		Lead II	0.30
		Lead III	0.15		Lead III	0.20
11	78	Lead I	0.20	88	Lead I	0.15
		Lead II	0.20		Lead II	0.20
		Lead III	0.10		Lead III	0.05

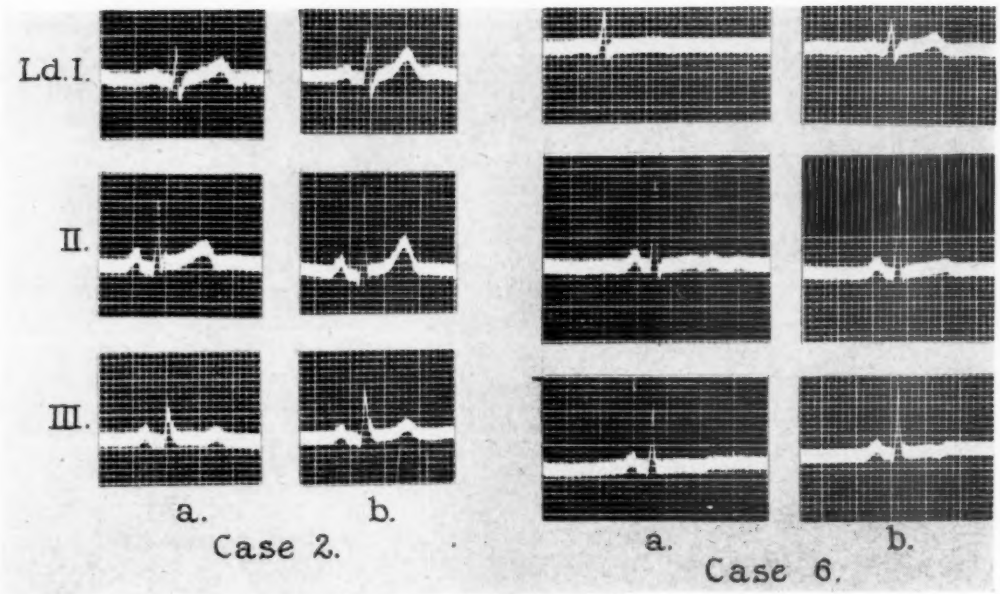

Fig. 1.

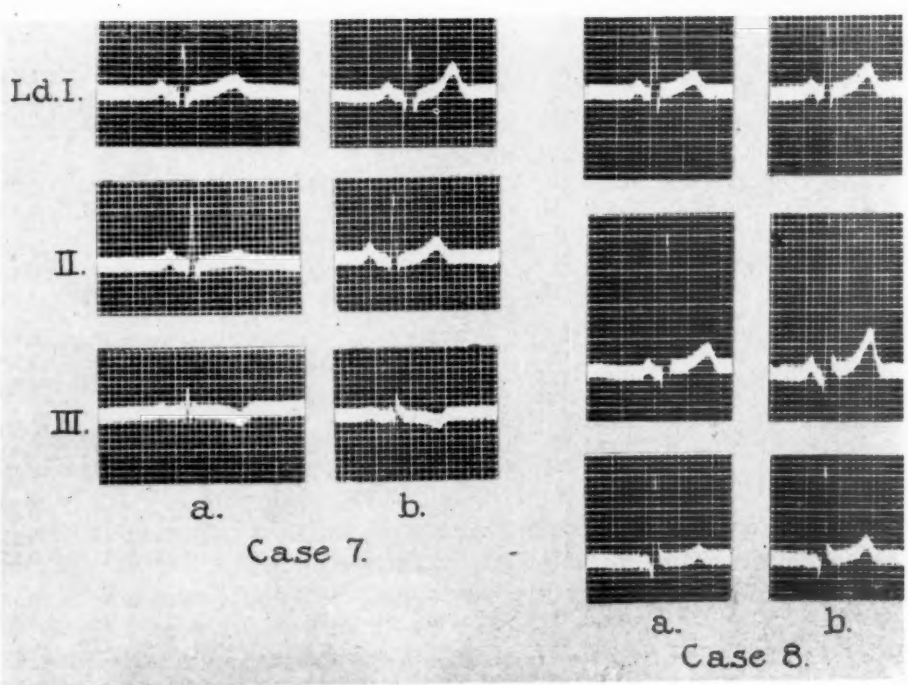

Fig. 2.

P-R Interval.—This, in all cases but one, was normal and was unchanged after recovery. In one case the P-R interval was 0.2 second during the disease and 0.16 second after recovery.

The QRS Complex.—There was a decrease in the voltage of the QRS complex in some of the cases. The QRS interval was unaltered.

Q-T Interval.—This was compared with the calculated value for the corresponding heart rate ($Q\text{-}T = K\sqrt{C}$). *K* was within normal limits during the disease and was unaltered after recovery (Table III). The normal value of *K* for males is 0.397 with a range of between 0.337 and 0.433.[1]

P Wave.—The P wave was normal in all cases except in Case 3, in which P_3 was inverted during the period of jaundice; it became upright after convalescence. In this case, the P wave was inverted again after exercise.

R-T Segment.—There was no change in the R-T portion of the curve.

T Wave.—In nine out of eleven records, the T wave was lower during the period of jaundice. This flattening of the T deflection was noted especially in Leads I and II. After convalescence was completed the T waves became normal and, in six cases, resembled records taken two years previously. In Figs. 1 and 2 are the electrocardiograms of four of the cases (*a*) during the height of the disease and (*b*) after recovery.

MECHANISM OF ACTION OF JAUNDICE ON THE HEART

Several possible factors in producing the electrocardiographic changes may be suggested. Bunting and Brown[2] reported finding, in the myocardium, hyalinization and necrosis of the cells, to which they attributed the death of their rabbits within twenty-four hours after the intraperitoneal injection of bile. Baltaceano and Vasiliu[3] ascribed the hypotension after the intraperitoneal injection of bile to the direct effect on the heart. Emerson[4] caused a fall in blood pressure, arrhythmia, and cardiac standstill in dogs following the intravenous injection of whole bile or bile salts. Horrall and Carlson[5] believed that bile salts act on the vagus endings and also directly on the myocardium through the coronary circulation. Regan and Horrall[6] noted a fall in blood pressure in dogs following the intravenous injection of sodium glycocholate. Still[7] demonstrated experimentally that the intravenous injection of small amounts of bile acids caused a slight rise in blood pressure and that large doses produced a marked fall. Ries and Still[8] decided that bile salts in small doses caused an increase in the irritability of the vagus endings in dogs, and that large doses blocked the same endings. Meltzer and Salant,[9] working on rabbits, affirmed Still's findings. Buchbinder,[10] working on puppies attributed the bradycardia experimentally produced to a reflex through the vagus. Baruk and Camus[11] believed that the bradycardia was due to bulbar intoxication. Wakim, Essex, and Mann,[12] working on denervated hearts (isolated) of rabbits, found that perfusion with preparations of bile salts and of whole bile resulted in a slowing of the heart rate, a diminution in the amplitude of contraction, and various cardiac disturbances (ventricular alternation, extrasystoles, and ventricular fibrillation). Working on dogs, they[13] concluded that whole bile and bile acids injected intravenously produced the same hypotensive effect and cardiac changes (brady-

cardia and disturbances in rhythm) in the absence, as well as in the presence, of the cardiac autonomic nerves. Schacter and Dworkin[14] concluded that the characteristic depressor action of bile salts in the circulating blood is not essentially due to the inhibition of cholinesterase.

Infectious jaundice is a generalized infection and the cardiovascular manifestation may be due to another factor, the direct involvment of the myocardium. Dawson and Hume[15] reported a case of spirochetal jaundice with paroxysmal auricular fibrillation. Marchal, Soulié, and Roy[16] reported, in the same condition, transient prolongation of the P-R interval and abnormal T waves. Electrocardiographic changes (paroxysmal auricular fibrillation, transient prolongation of the P-R interval, and flattening or inversion of the T waves[15-18]) have been noted in cases of spirochetal jaundice. In Weil's disease, pathologic changes (parenchymatous and interstitial changes with nuclear swelling, chromatolysis, infiltration of the interstitial tissue by lymphocytes, and polymorphonuclear leucocytes) have been described in the myocardium. Other observers have noted perivascular cellular infiltration, vacuolization, loss of striation, and hyalinization of the muscle bundles, acute leptospiral vegetative endocarditis, spirochetes in the myocardium, and multiple hemorrhages in the pericardium, subepicardium, and myocardium.[19-27]

EFFECT OF EXERCISE ON THE SIZE AND SHAPE OF THE T WAVE

Because it was suggested that the T-wave changes noted in the eleven cases of infectious jaundice might be due to changing heart rate, the eleven subjects were studied several months after recovery. Electrocardiograms were taken after a thirty-minute rest period and after twenty-five to thirty vigorous hops. The data of this study are summarized in Table IV. It can be seen that, after exercise, the T waves became smaller (in at least two leads) in nine out of the eleven cases. In one case there was no change. In one case there was an increase in two leads; the increase was most noticeable in Leads I and II.

In another group of eleven normal persons, the height of the T wave was lowered by exercise in six cases; in four cases the T wave was increased in amplitude; and in one case there was no change. Thus, in a total of twenty-two controls, including the eleven cases of the series here reported (after recovery), tachycardia lowered the T wave in fifteen and increased it in five. The effect of exercise on the T wave was studied by Wood and Wolferth,[29] and their conclusion was that exercise caused an elevation in some controls and a depression in others. Clough[30] and Levine et al.[31] studied the electrocardiograms after the subcutaneous injection of epinephrine and found in most instances a decrease in the height of the T wave at the time of the maximum epinephrine effect. In the cases of jaundice, the T wave was reduced in amplitude although bradycardia was usually present. Therefore change in the heart rate was not responsible for the decrease in amplitude of the T deflection.

SUMMARY

1. In an epidemic of twenty-four cases of infectious hepatitis, eleven subjects were studied electrocardiographically at the height of the disease and after recovery.

2. In nine cases the T wave was depressed during the disease and became normal after recovery.

3. There was no correlation between the depression of the T wave and the height of the fever or the intensity of the jaundice.

4. A study of a control group of persons after exercise revealed a depression of the T wave (with acceleration of heart rate), thus showing that the bradycardia was not responsible for the electrocardiographic changes.

5. A review of the reports of experiments in which bile salts and whole bile were injected into animals revealed similar T-wave changes which were probably due to an effect either on the vagus endings in the heart or on the myocardium itself. The myocardial effect is probably important in cases of Weil's disease, as evidenced by the reported pathologic findings in the myocardium.

Miss Olive Park and Miss Marjorie Frasier assisted in the technical work, and we are indebted to them.

REFERENCES

1. Shipley, R. A., and Hallaran, W. R.: The Four-Lead Electrocardiogram in Two Hundred Normal Men and Women, AM. HEART J. 11: 325, 1936.
2. Bunting, C. H., and Brown, W. H.: The Pathology of Intraperitoneal Bile Injections in the Rabbit, J. Exper. Med. 14: 445, 1911.
3. Baltaceano, G., and Vasiliu, C.: Le taurocholate de sodium et les zones réflexogènes sinocartidiennes, Compt. rend Soc. de biol. 115: 1552, 1934; 116: 550, 1934.
4. Emerson, W. C.: Toxic Constituent of Bile, J. Lab. & Clin. Med. 14: 635, 1929.
5. Horrall, O. H., and Carlson, A. J.: Toxic Factor in Bile, Am. J. Physiol. 85: 591, 1928.
6. Regan, J. F., and Horrall, O. H.: Physiologic Action of Dehydrocholic Acid, Am. J. Physiol. 101: 268, 1932.
7. Still, E. U.: On the Toxicity of Purified Bile Preparations, Am. J. Physiol. 88: 729, 1929.
8. Ries, F. A., and Still, E. U.: Toxicity of Purified Bile Preparations; Influence on Cardiovascular Responses, Arch. Int. Med. 51: 90, 1933.
9. Meltzer, S. J., and Salant, W.: Studies on the Toxicity of Bile. I. The Effects of Intravenous Injections of Bile Upon Blood Pressure, J. Exper. Med. 7: 280, 1905; II. The Toxic Effects of Bile Upon the Central Nervous System and the Elimination of Strychnine Through the Bile in Nephrectomized Animals 8: 127, 1906.
10. Buchbinder, W. C.: Experimental Obstructive Jaundice; Age Factor in Production of Bradycardia, Arch. Int. Med. 42: 743, 1928.
11. Baruk, H., and Camus, L.: Action neurotrope expérimentale de biles humaines, recueillies par tubage duodénal chez chat, la souris, le pigeon et le cobaye, Compt. rend. Soc. de biol. 116: 27, 1934.
12. Wakim, K. G., Essex, H. E., and Mann, F. C.: The Effects of Whole Bile and Bile Salts on the Innervated and the Denervated Heart, AM. HEART J. 20: 486, 1940.
13. Wakim, K. G., Essex, H. E., and Mann, F. C.: The Effects of Whole Bile and Bile Salts on the Perfused Heart, AM. HEART J. 18: 171, 1939.
14. Schacter, M., and Dworkin, S.: On Cardiovascular Action of Bile Salt With Regard to Inhibition of Cholinesterase, Am. J. Physiol. 137: 599, 1942.
15. Dawson, B., and Hume, W. E.: Jaundice of Infective Origin, Quart. J. Med. 10: 80, 1917; idem., Brit. M. J. 2: 345, 1917.
16. Marchal, G., Soulié, P., and Roy A.: Spirochètose ictéro-hémorragique. Troubles Cardiaques et Modifications electrocardiographiques, Bull. et mém. Soc. méd. d. hôp. de Paris 51: 1651, 1935.
17. Clapper, M., and Myers, G. B.: Clinical Manifestations of Weil's Disease With Particular Reference to Meningitis, Arch. Int. Med. 72: 18, 1943.
18. Hume, W. E., and Szakely, P.: Cardiac Involvement in Spirochaetal Jaundice, Brit. Heart J. 6: 135, 1944.
19. Mollaret, P., and Ferroir, J.: A propos de deux observations de spirochitose ictérohémorragique, dont une avec myocardite mortelle. Contribution à l' étude de la réaction méningée des formes typiques ictérigènes, Bull. et mém. Soc. méd. d. hôp. de Paris 51: 1622, 1935.
20. Beitzke, H.: Ueber die pathologische Anatomie der ansteckenden Gelbsucht (Weilsche Krankheit), Berl. klin. Wchnschr. 53: 1313, 1916.

21. Ashe, W. F.; Pratt-Thomas, H. R., and Kumpe, C. W.: Weil's Disease; Complete Review of American Literature and Abstract of World Literature; 7 Case Reports, Médicine 20: 145, 1941.
22. Drägert, E.: Beitrag zur pathologischen Anatomie der Weilschen Erkrankung, Virchows Arch. f. path. Anat. 292: 452, 1934.
23. Kaneko, R., and Okuda, K.: The Distribution in the Human Body of Spirochaeta Ictero-hemorrhagiae, J. Exper. Med. 26: 325, 1917.
24. Ryle, J. A.: Weil's Disease, Brit. M. J. 2: 413, 1916.
25. Watson, G. W., McCleod, J. W., and Stewart, M. J.: Fatal Case of Leptospiral Jaundice of Obscure Origin, Brit. M. J. 1: 639, 1935.
26. Swan, W. G. A., and McKeon, J. A.: Weil's Disease Among Coal Miners in Northumberland and Durham, Lancet 2: 570, 1935.
27. Jeghers, H. J., Houghton, J. D., Rae, J. H., and Foley, J. A.: Weil's Disease. Report of a Case With Postmortem Observations and Review of Recent Literature, Arch. Path. 20: 447, 1935.
28. Davidson, L. S. P., and Smith, J.: Weil's Disease in Fish-Workers: Clinical, Chemical and Bacteriological Study of 40 Cases, Quart. J. Med. 5: 263, 1936.
29. Wood, F. C., and Wolferth, C. C.: Angina Pectoris; Clinical and Electrocardiographic Phenomena of Attack and Their Comparison With Effects of Experimental Temporary Coronary Occlusion, Arch. Int. Med. 47: 339, 1931.
30. Clough, H. D.: Effects of Epinephrin on Electrocardiograms of Patients With "Irritable Heart," Arch. Int. Med. 24: 284, 1919.
31. Levine, S. A., Ernstene, A. C., and Jacobson, B. M.: Use of Epinephrine as Diagnostic Test for Angina Pectoris With Observations on Electrocardiographic Changes Following Injections of Epinephrine Into Normal Subjects and Into Patients With Angina Pectoris, Arch. Int. Med. 45: 191, 1930.

A METHOD FOR THE CONSTRUCTION OF THE VECTORCARDIOGRAM FROM THE EINTHOVEN ELECTROCARDIOGRAM

FREDERICK H. HOWARD, M.D.
NEW YORK, N. Y.

THE term "vectorcardiogram" was applied by Wilson and Johnston[1] to a kind of record which shows in a single tracing the variations of the electric field within the body during the heartbeat. The record is made by means of a cathode-ray tube so connected to the Einthoven limb electrodes that the potential differences at the surface points combine to control the electron beam in such a way that the movements of the light spot on the fluorescent screen represent the changes in the direction and intensity of electric force due to the heart's activity. During diastole, when there are no potential differences in the heart, the spot of light remains stationary at the center of the screen. When activation of the heart muscle occurs and potential differences arise, the light spot is displaced to a succession of new positions which represent by direction and distance from the center the changing orientation and intensity of the electric field. The light spot finally returns to the center of the screen as the electric field fades at the end of the systole. The tracing consists of two loops of irregularly elliptical form, one being inscribed during the QRS period, the other during the T period. The latter is continuous with the former at a point which usually lies near the center of the screen. The electrical effects of auricular activity cause a similar but rather small displacement of the electron beam, but this effect, which is of less importance than is that produced by the ventricles, will be omitted from the present discussion. The movement of the light spot recorded on photographic film constitutes the vectorcardiogram. In this paper it will be referred to as the "VC." For examples of such records the reader is referred to Fig. 8.

During four years prior to 1940 the technique of vector representation of the heart's electric field was developed actively in Germany. By means of cathode-ray apparatus, connected to surface electrodes in one manner or another, several investigators[2-10] produced records of different types and called by various names (Vektordiagramm, Triogramm, etc.) and had commenced a study of their clinical significance. In the comprehensive paper published early in 1940, Schellong[5] reviewed the work of others and reported his own investigations, while the paper by Hollmann and Guckes[9] dealt with the more important clinical interpretations, as well as with the technique.

It must be emphasized that the VC discloses nothing but that which is implicit in the electrocardiogram. When the potential differences between the electrodes in each lead are recorded separately, the electrocardiogram is pro-

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duced. If, on the other hand, these three potential differences are combined suitably by instrumental means, the result, a VC, is a unitary record to which each of the three leads makes a contribution determined by the geometric relation of the lead to the actual electric field. In brief, the electrocardiogram may be said to analyze the field of electric force into three components, while the VC apparatus serves to recombine these components into a single unitary view of the field.

The true VC is, of course, a space curve, for the electric field of the body is extended in three dimensions in space; but, since the electrocardiogram is derived from potential differences measured only in the frontal plane of the body, the VC is a frontal plane projection of the true spatial VC. It is possible to derive the spatial VC by means of special records made by the cathode-ray apparatus and viewed stereoscopically. The German investigators previously referred to gave much attention to this stereoscopic technique and produced an interesting and probably important type of record. However, this phase of vectorcardiography will not be considered here since our concern is merely with a method of translating the electrocardiogram into the related frontal plane VC.

Since the VC is a product of the instrumental synthesis of the potential differences occurring in the three electrocardiographic leads, it is to be expected that the same curve could be derived by analytic or graphic treatment of quantities given by measurements made on the electrocardiogram. The object of the present paper is to describe a method by which this translation of an electrocardiogram into a VC may be made graphically with a minimum of effort and time, yielding a useful approximation to the exact VC.

In 1920, Mann[11] described the mathematical relationship between the electrocardiogram and a constructed curve, called by him a "monocardiogram," representing the variation of the electric field during the heartbeat. I believe Mann was the first to employ a tracing of the terminus of the changing vector to represent the successive vectors themselves, although Lewis, several years previously, and perhaps others before him, had employed diagrams picturing the vector at successive instants by means of lines radiating from a common center like the ribs of a fan. Mann's method provides a tracing which faithfully represents the vector changes, but the technique is tedious and time-consuming. Mann, himself, stated that the drawing of one monocardiogram "involved many hours of careful work," and it is probable that the neglect of his method has been due to the impracticability of employing the method in numerous cases, rather than to doubt about the value of the information that might have been derived. The method to be described here has been developd in the hope that its facility may lead to frequent employment and to discovery of meaning in the VC not apparent in the electrocardiogram. The possible usefulness of the VC method can be tested adequately only by its application to a large number of cases, and for this a facile method is needed. No doubt the cathode-ray apparatus, connected through the network devised by Wilson, provides the ideal means, but the apparatus at present is available only to a few

investigators. However, in one respect, the constructed VC has an unique advantage over the recorded VC: the analysis may be applied to electrocardiograms of selected types chosen from the store of existing records, and thus the investigator rapidly may accumulate data which may be treated statistically.

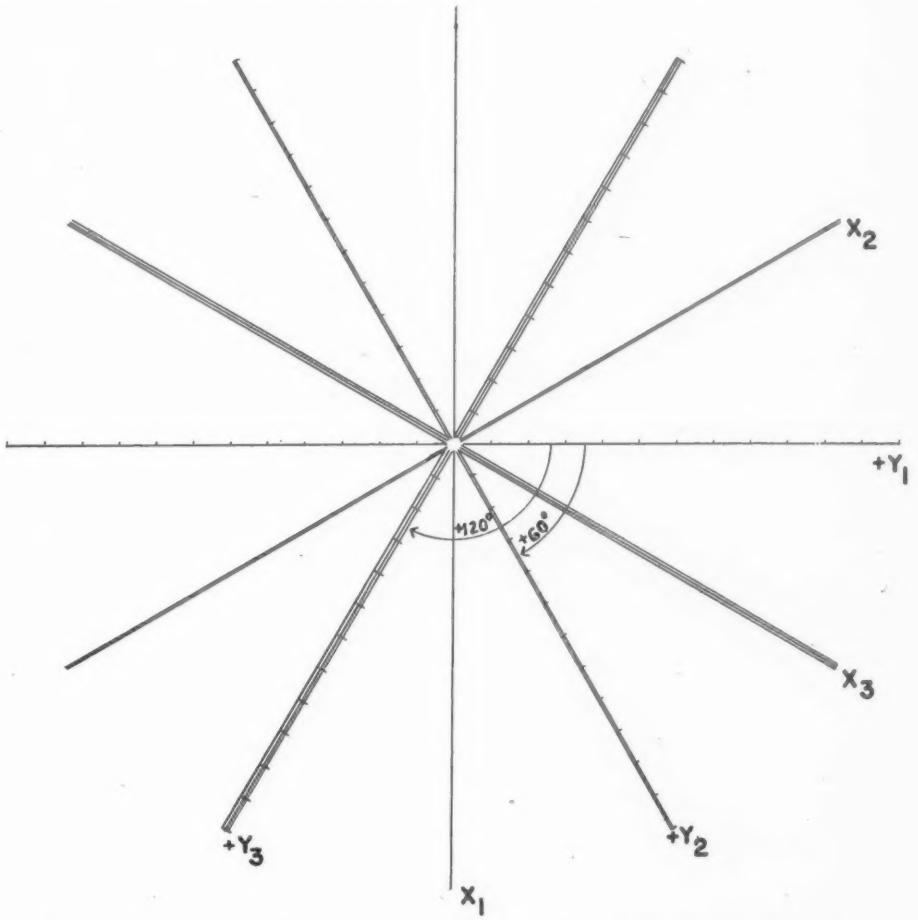

Fig. 1.—The threefold reference system. Each x axis divides the whole field into a positive and a negative half for the plotting of positive and negative potentials recorded in the respective lead tracings. The positive and negative y axes serve for the measurement of the departure of the QRS and T loops from the respective x axes. Scale on y axis: 1 unit = 0.1 millivolt.

THE METHOD OF CONSTRUCTING THE VECTORCARDIOGRAM

The principle of the method of construction is implicit in the well-known diagrams, published by many authors, showing the relation of the three lead tracings to the vector of the electric field framed in the Einthoven equilateral triangle. It is unnecessary here to attempt a justification of the Einthoven hypothesis in order to give validity to the VC. It is not claimed that the VC is a true graph of vector behavior; it is no more than an integrated view of the electrocardiogram. The integration, it is true, is based on the

Einthoven assumptions, but, even if these assumptions do not correspond closely to the facts, the hypothesis may be adopted arbitrarily as a means of arriving at a unitary view of the three electrocardiographic leads, which then may be correlated usefully with pathologic states and processes of the heart.

The frame of reference within which the VC is to be drawn consists of six lines intersecting at a common point, the origin, and separated by angular intervals of 30 degrees. These six lines, grouped in three pairs, form three overlapping reference systems, each of which serves for the representation of the potential differences recorded by one of the three leads of the electrocardiogram (Fig. 1). Distances and angles in this reference frame will be called positive or negative in a sense conforming with long-established electrocardiographic practice. Thus, distances measured to the right or downward will be called positive, while those measured in the opposite direction will be considered negative. Angular intervals measured clockwise will be called positive, while those that are measured counterclockwise will be considered negative.*

The co-ordinate axes for Lead I are the horizontal at 0° and the vertical at 90°. The vertical line serves as an x_1 axis, and distances measured from this line to the right represent positive potentials found in Lead I, whereas negative potentials are plotted to the left of the vertical. Distances from the x_1 axis may conveniently be measured along the horizontal by means of a scale marked upon it, 1 cm. on the scale representing 0.1 mv., or 1 mm. on a correctly standardized electrocardiographic tracing. The horizontal properly may be called the y_1 axis, for it is along this axis that the ordinates, or amplitude values of the electrocardiographic tracing, are measured. The x_1 axis, at 90°, bears no scale, for there is no electrocardiographic quantity requiring representation in this direction. The x_1 axis serves, however, to divide the whole field into a positive and a negative half with respect to Lead I. The second lead potentials, if positive, are represented by distances measured downward and to the right of the field from the x_2 axis at 150° in the direction of the y_2 axis at 60°. Negative potentials in Lead II are, of course, measured from the x_2 axis in the opposite direction. Lead III potentials are represented similarly by reference to the x_3 axis at 30°, positive and negative potentials being measured off from the x_3 axis in the 120° and the –60° directions, respectively. Although these three coordinate systems overlap, each is independent of the others and singular to the lead which it serves.

For some purposes it is desirable to define points on the VC by means of the ordinary rectangular co-ordinates. For this purpose the horizontal at 0° serves as a positive x axis, while that at 90° serves as a positive y axis.

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*It seems inadvisable, in electrocardiographic studies, at this time, to adopt the mathematical convention whereby angular intervals that are extended counterclockwise are called positive. The wide adoption of this so-called English system by mathematicians and physicists probably was due to its adaptability to the mathematical treatment of electromagnetic phenomena, developed especially by English physicists; but this argument seems to have little weight in electrocardiographic studies. It perhaps is not widely known that the English system has no universal sanction; French mathematicians formerly called clockwise motion positive, or were eclectic in the matter, choosing whichever designation suited the purpose in hand. It may be that the English system serves better when the treatment of electrocardiographic problems is extended into the field of mathematical physics, as in some of the writings of Wilson and of Bayley, but for the simpler analyses, such as those of this paper, the system which was employed by Einthoven and, since then, has been in general use, seems better suited. Since the mean vector in normal cases is directed downward it is convenient and natural to use the positive sign for angular intervals measured downward from the horizontal axis.

It will be seen at once that this method of representing electrocardiographic potentials is strictly consistent with the Einthoven scheme. The y_1 (0°), y_2 (60°), and y_3 (120°) axes are parallel, respectively, to the three sides of the equilateral triangle. Positive angular intervals are measured clockwise from the horizontal axis and positive potentials are measured in the 0°, 60°, and 120° directions.

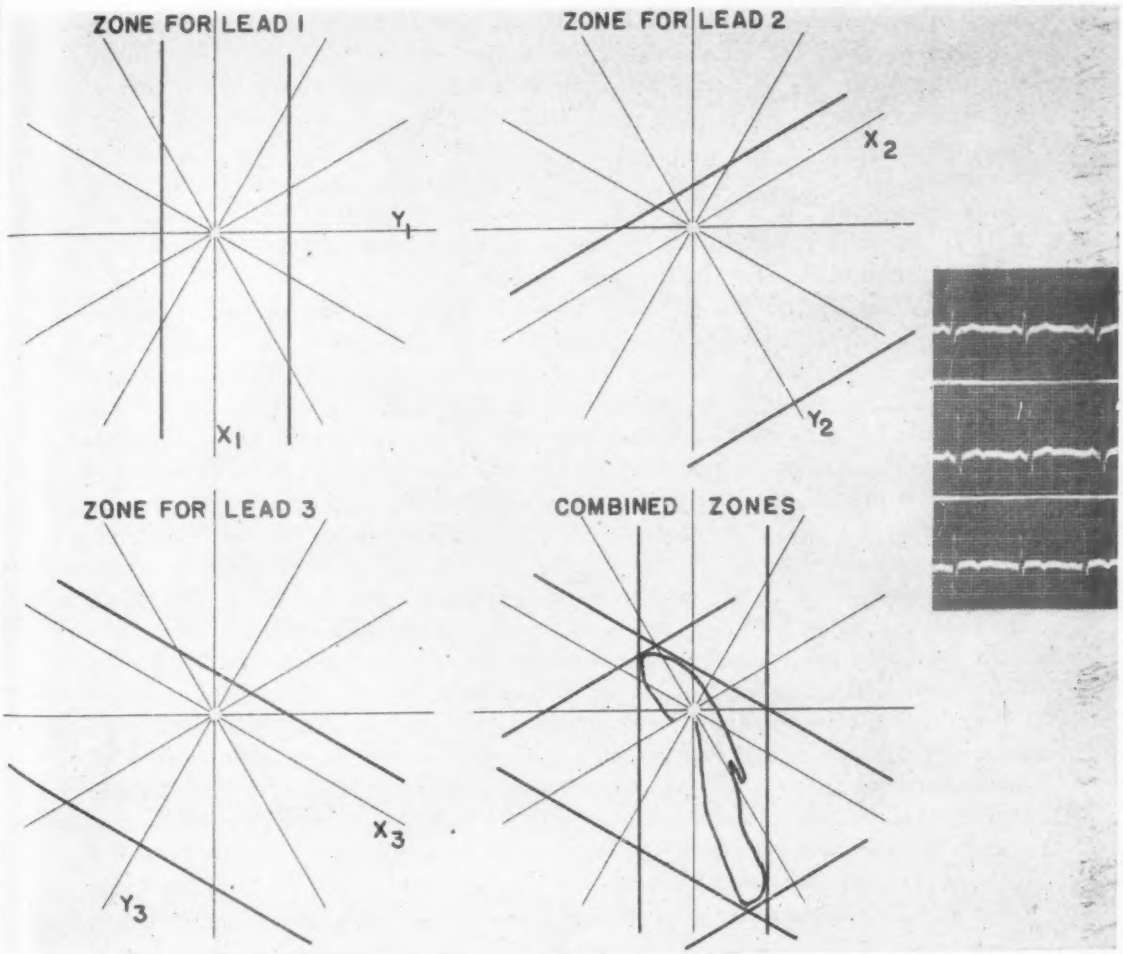

Fig. 2.—The composition of the polygonal envelope of the QRS loop is effected by combining the three zones that define the potentials recorded in the respective leads.

The approximate VC is drawn in this co-ordinate system in the manner now to be described. The equipment necessary for the work is simple. Two draftman's triangles, each having angles of 30°, 60°, and 90° are needed. The origin should be placed somewhat to the left of the center of a sheet of paper 8 by 10 inches. The six axes are readily drawn by suitable manipulation of the triangles. The y axes should be graduated in centimeters, each centimeter representing 0.1 millivolt. If much work is to be done time is saved by the use of

mimeographed forms. Dividers may be used to measure amplitudes in the electrocardiogram, but this is not necessary since visual estimates give as much precision as the work calls for.

The maximum positive and negative voltages of the QRS complex in each lead tracing are measured and plotted as points on the proper y axes. Through each of these points a line is drawn at right angles across the y axis (Fig. 2). For each lead there will be two such lines. Each pair of lines defines a zone the length of which is unlimited but whose lateral boundaries represent the positive and negative limits of amplitude shown in the respective electrocardiographic lead. Therefore, the VC must lie within each zone and be tangent to the lateral boundaries of each. Consequently, the VC must lie in the area common to the three zones and be tangent to each of its boundaries. This common area is a six-sided polygon, constituting an envelope of the VC. Although the tangent points are not defined, the polygon, nevertheless, reveals the general shape of the VC and its orientation in the field. An enveloping polygon outlining the T loop is to be constructed in the same manner.

The VC might be defined more closely if the maximum and minimum potentials along other axes also were to be recorded by the electrocardiograph. It is possible to accomplish this by a simple maneuver (Fig. 3). If the electrode on the left arm and that on the left leg are connected through a resistance of, say, 5,000 ohms the potential at the mid-point of the resistance will be equal to the mean of the potentials at the left arm and the left leg. Now, if the mid-point be connected through a galvanometer with the right arm electrode, an electrocardiogram may be recorded which represents proportionally the difference in potential along an axis midway between that of Lead I and Lead II, that is, an axis at 30°. The magnitude of the voltages recorded will be somewhat less than that appropriate to a true 30° lead, but the full theoretic values for a 30° lead may be obtained by multiplying the recorded voltages by the factor $2/\sqrt{3}$, or 1.15. Similarly, a pseudo-90° tracing may be made by connecting the mid-point of a resistance between the right and the left arm through the galvanometer to the left leg. A third interpolated lead, recording the proportional voltage in the 150° direction, requires a resistance between the right arm and the left leg and a connection from its mid-point through the galvanometer to the left arm. If, now, the maximum and minimum potentials recorded by these interpolated leads be measured and each multiplied by 1.15, the three pairs of values so obtained may be used to locate six more sides to be added to the polygon enveloping the VC. The twofold increase in the number of sides increases the accuracy with which the VC may be drawn, but this accuracy is gained only at the cost of time and effort when the electrocardiogram is recorded, so that the method probably would not be acceptable for clinical routine but only for special studies.

The VC now is traced within the polygonal envelopes constructed for the QRS complex and for the T wave, respectively. The QRS loop is begun at the center of the field and continued as a smooth curve, grazing in succession each side of the polygon. The method does not provide any simple means of determining the tangent points on the six sides, but some considerations which may serve

as a partial guide will be mentioned later. An acquaintance with the patterns of recorded VC loops published by Wilson and Johnston[1] (Fig. 8) can be of assistance. The QRS loop ends at the origin or at a near-by point, the location of which is discussed below. From this point the T loop is drawn in like manner within the small polygon previously drawn to represent the maximum and minimum voltages of the T deflection. As will be apparent later, the direction of motion of the vector is of importance, but the form of the VC is independent of the direction in which it is traced. Hence the curve should be drawn either clockwise or counterclockwise, as appears convenient. The direction of rotation then can be determined by methods which will be explained in a later section.

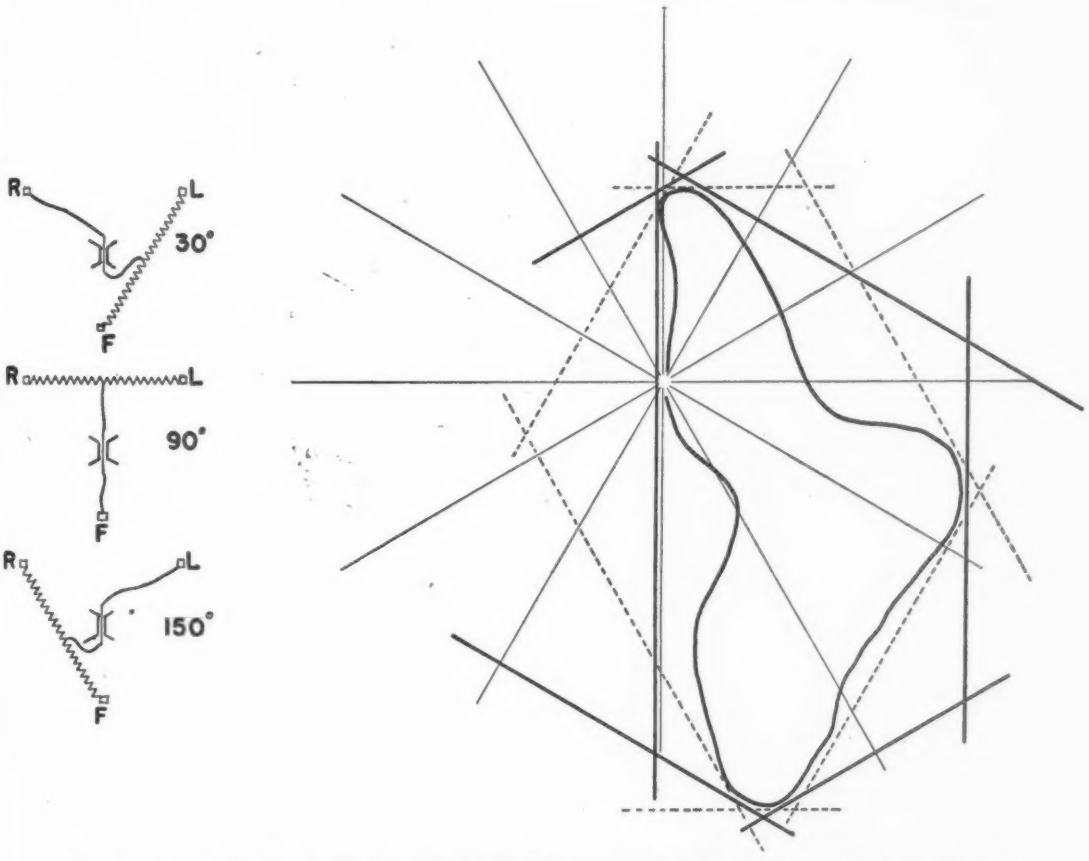

Fig. 3.—The twelve-sided envelope for the QRS loop is formed by adding to the basic polygon six lines representing the potential limits recorded by means of *interpolated leads.*

The point at which the end of the QRS loop joins the beginning of the T loop is of considerable importance. It will be referred to as *J* (for junction). The corresponding point in the electrocardiogram also will be called *J*.*

*The symbol *J* might well be substituted in electrocardiographic terminology for the official term "R-T junction" or for terms inspired by an excess of zeal for precision, such as "the R-T or S-T junction as the case may be," a designation actually used by one author. The thing to be designated is only a point, and should be indicated by a letter; the component of QRS which ends at the point should be omitted from the general term used to indicate the point.

To locate J in the vector field the position of J in each electrocardiographic lead first is identified and then its displacement from the zero level is measured. This procedure sometimes is difficult on account of the ill-defined transition of the QRS complex to the T deflection, or because of uncertainty of the zero level, or, again, because of the variability of the complexes due to respiratory or other less obvious causes. But, if care is taken, the result will be found very nearly to satisfy Einthoven's summation equation, $e_2 = e_1 + e_3$. Turning now to the VC field, a point is selected on each of the three y axes corresponding to the respective potentials of J in the electrocardiogram. Through each of these points a line is drawn perpendicular to its proper y axis. If the displacements of J in the electrocardiogram have been measured correctly the lines will intersect at a point, a necessary consequence of the summation equation; but more often they will form a small equilateral triangle the size of which will be proportional to the errors in measuring the displacement of J in the electrocardiogram. If the triangle is small a point at its center may be taken as the approximately correct position of J.

The VC, having been sketched in roughly, should be scrutinized, segment by segment, to see if it is, in all parts, consistent with the potential changes revealed by the electrocardiogram. It is obvious that, where the potential is increasing in a segment of one lead, the departure of the corresponding segment of the VC from the x axis proper to that lead also must be increasing. But it is necessary that this representation of the sign and rate of change of potential should be true with respect to all three leads simultaneously. If it were possible perfectly to fulfill this requirement the VC would be a quite faithful representation of all that is shown in the electrocardiogram, but, of course this ideal result is beyond reach. However, it will be found that the simultaneous control of the path of the VC by three leads is not too difficult to visualize and that, with a little practice, the roughly sketched VC can be rectified to yield useful results.

Theoretically, notching and slurring of QRS can be represented in the VC, but it was found in practice that such representation was not very satisfactory when compared with the cathode-ray record. Unless the faulting is very coarse it is better to neglect it. Whether or not this limitation is a desideratum from the clinical standpoint cannot well be judged until the clinical meaning of short-period variations of potential are better understood.

THE DEVELOPMENT OF DETAIL IN THE CONSTRUCTED VC

A study of the mathematical relationship of the VC to the electrocardiogram reveals several additional characteristics of the loops that may be deduced from the Einthoven record. First, it is possible by rather simple means to determine the direction of the VC curve in any particular segment, and thus to correct the roughly drawn loop to any desired extent, within modest limits. Second, the direction in which the loop is inscribed may be determined with certainty in most cases. Third, the velocity of inscription of particular segments may be determined approximately. All these characteristics may be determined by Mann's method, but that technique seems too burdensome to be acceptable. New

methods will be described here by which these details may be revealed, and it is believed that the methods are facile enough to commend themselves to anyone not aversé to a little computation.

It must be acknowledged that no great accuracy can be obtained by these methods, but it is thought that the approximation can be made close enough to give results of some practical value. Accuracy is unobtainable primarily because the time element, clearly expressed in the electrocardiogram, is largely submerged and lost in the process of constructing the VC, so that it is impracticable to identify on the VC a point representing a particular time instant on the electrocardiogram. However, it is possible to correlate segments of the VC with nearly simultaneous segments of the electrocardiogram. Thus, early, middle, and late segments of the excursive (outgoing) limb of the VC loop readily are correlated with corresponding segments of the ascending limb of the electrocardiographic deflection, and as one becomes accustomed to the technique, the simultaneous segments may be defined with increasing confidence. Another characteristic of the ordinary electrocardiogram makes great accuracy unobtainable; the record made by a galvanometer with only one string necessarily requires that the three leads be recorded in succession, and thus one does not have a first and second lead record of one particular heartbeat; consequently when a second lead deflection is paired with another in the first lead it is by no means certain that the two are strictly congruous.

DETERMINATION OF THE SLOPE OF A SEGMENT OF THE VC

To determine the direction, or slope, of a particular segment of the VC use is made of an electrocardiographic characteristic which, I believe, previously has not been considered in electrocardiographic studies, i.e., the slope of the electrocardiographic tracing at a particular point. It can be shown that the slopes at simultaneous points on the tracings of two electrocardiographic leads determine the direction, or slope, of the corresponding segment of the VC. The mathematical analysis disclosing this relationship follows immediately. We assume that the approximate VC has been drawn. For the rectification of a particular segment it is desired to find the average slope of the curve in that region. The slope of the VC at any point is that of the tangent with reference to the horizontal and vertical axes constituting the x and y axes of a rectangular co-ordinate system. The tangent may be expressed as y/x, but since the direction of the curve is continually changing we will express the slope by the differential notation dy/dx. In the analysis the following symbols also will be used.

E_m, the magnitude of the vector at any point on the VC.

e_1 and e_2, the amplitude (voltage) of the electrocardiographic tracing in Leads I and II, respectively.

de_1 and de_2, differentials standing for the slopes of the electrocardiographic tracings at corresponding points in Lead I and Lead II.

x the distance of any point on the VC from the vertical axis.

y the distance of any point on the VC from the horizontal axis.

α the angle between the vector and the horizontal axis at any instant.

t time as measured on the electrocardiographic tracing.

The analysis begins with the familiar equations of Einthoven,

$$e_1 = E_m \cos \alpha \qquad (1)$$

$$e_2 = E_m \cos (60° - \alpha) \qquad (2)$$

From these we derive equations giving the value of x and y in terms of e_1 and e_2 with the angle α eliminated. From the definitions and from the construction it is evident that

$$x = e_1 \qquad (3)$$

From Equation 2, by suitable transformation* we have

$$y = \frac{1}{\sqrt{3}} (2e_2 - e_1) \qquad (4)$$

By differentiation of Equations 3 and 4, with respect to time, we obtain

$$\frac{dx}{dt} = \frac{de_1}{dt} \qquad (5)$$

$$\frac{dy}{dt} = \frac{1}{\sqrt{3}} \left(\frac{2de_2 - de_1}{dt}\right) \qquad (6)$$

Dividing Equation 6 by Equation 5 and replacing $\frac{1}{\sqrt{3}}$ by 0.58

$$\frac{dy}{dx} = \frac{1}{\sqrt{3}} \left(\frac{2de_2}{de_1} - 1\right) \qquad (7)$$

By similar steps, employing the slopes measured in Lead I and Lead III, we obtain

$$\frac{dy}{dx} = \frac{1}{\sqrt{3}} \left(\frac{2de_3}{de_1} + 1\right) \qquad (8)$$

and from Lead II and Lead III,

$$\frac{dy}{dx} = \frac{1}{\sqrt{3}} \left(\frac{de_2 + de_3}{de_2 - de_3}\right) \qquad (9)$$

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*The steps in the transformation are as follows: By the standard formula for the cosine of the difference of two angles Equation 2 may be written

$$e_2 = E (\cos 60° \cos \alpha + \sin 60° \sin \alpha)$$

$$\text{or } e_2 = \tfrac{1}{2} E \cos \alpha + \frac{\sqrt{3}}{2} E \sin \alpha$$

Transposing, $\frac{\sqrt{3}}{2} E \sin \alpha = e_2 - \tfrac{1}{2} E \cos \alpha$

Dividing by $\frac{\sqrt{3}}{2}$ and factoring,

$$E \sin \alpha = \frac{1}{\sqrt{3}} (2e_2 - E \cos \alpha)$$

From the construction, $E \sin \alpha = y$, while by Equation 1 $E \cos \alpha = e_1$

Hence by substitution, $y = \frac{1}{\sqrt{3}} (2e_2 - e_1)$

Method of Using the Slope Equations.—Any one of the three pairs of leads may be used for the determination of the slope of a particular segment of the VC, but usually one pair is best suited for measurement; this should be chosen, and the proper equation used. The slope of the electrocardiographic tracing at a selected point may be measured easily in the following manner (Fig. 4): The straight edge of a piece of paper is placed accurately tangent to the tracing at the selected point. A small protractor is then placed so that its base edge coincides with any convenient horizontal line of the electrocardiographic grid, the center mark of the protractor being placed at the edge of the paper. Then,

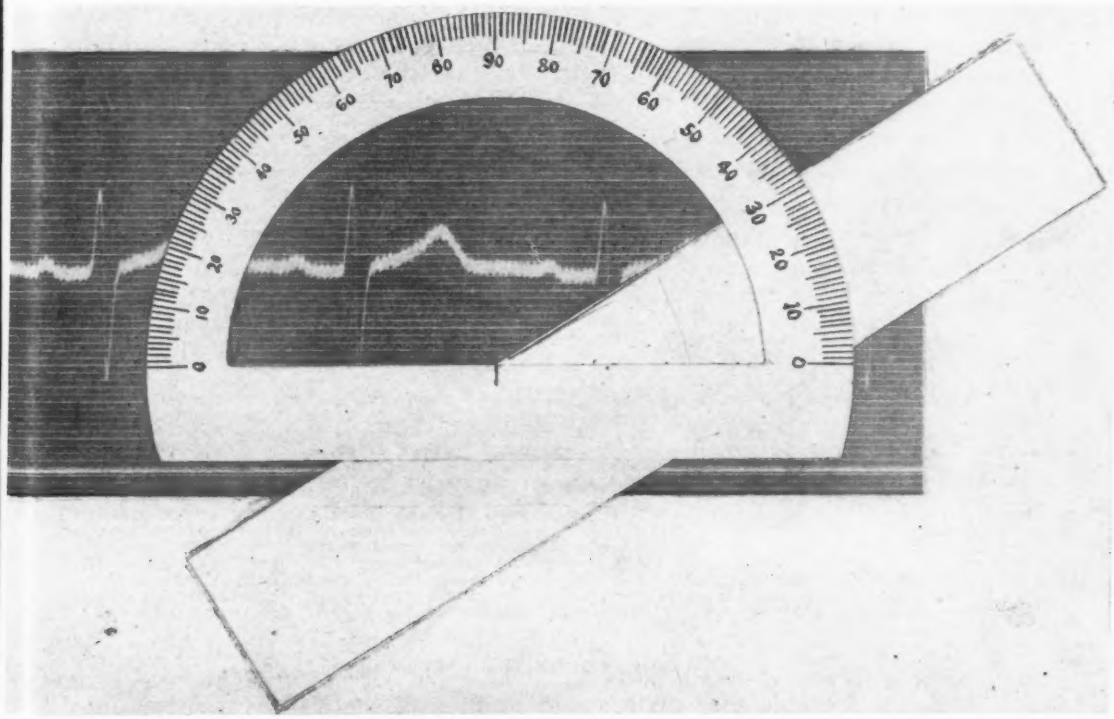

Fig. 4.—Showing the method of measuring the slope of a segment of electrocardiographic tracing by means of a protractor and a paper straightedge.

on the scale of degrees, the angle between the edge of the paper and the horizontal grid line is read off. A table of trigonometric functions is used to find the tangent of the angle, that is, the slope of the electrocardiogram at the point in question. There remains only the substitution of the values found in the two leads for the differentials in the proper slope equation (Equation 7, 8, or 9) and completion of the indicated calculation. The result is the slope of the tangent to the VC. Usually it will be convenient to find the angle represented by the tangent and to use the angle to indicate the direction of the curve.

From the slope equations simple relations may be deduced by means of which it is practicable roughly to determine the slope of the VC without the use of measurements or calculations, the necessary data being obtained by mere

inspection of the electrocardiogram. These relations are set forth in Fig. 5. The diagram provides data for a rough check on the correctness of the value of the slope obtained by measurements and calculation, but, more especially, it is useful for revising the original rough sketch of the VC.

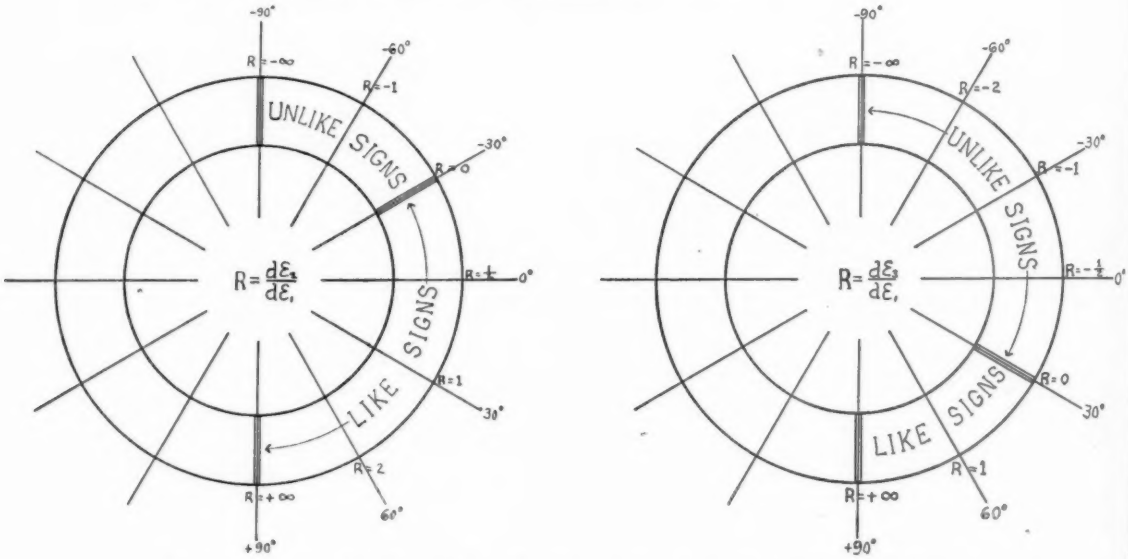

Fig. 5.—Diagrams for the rough estimation of the slope of a segment of the VC. The diagrams show the slope, dy/dx expressed as angle, of a segment of the VC when the ratio, de_2/de_1 or de_2/de_1, has the indicated value. The ratios of the slopes of the electrocardiographic tracings are represented by the symbol R. The corresponding slope of the VC is shown in one or the other indicated sector depending on the sign of the ratio. The value of R varies continuously from $-\infty$ to $+\infty$. For approximate results intermediate values of R may be interpolated visually. Use of the diagram may be illustrated as follows: if the slope of segment of the electrocardiogram in Lead II is about twice as great as the slope of the corresponding segment in Lead I the $R = 2$; if the slopes of the segments of the electrocardiogram are both positive or both negative, then the slope of the corresponding segment of the VC will be shown in the first diagram by the radius in the sector of like signs where $R = 2$. This slope is 60°. These diagrams must not be mistaken for representations of the vector field with the radii as vectors of electric force; the radii represent merely the slope of a segment of the VC, and the segment in question may lie in any part of the vector field.

THE ROTATION OF THE VECTOR

It seems probable that the sense of rotation of the VC* is a significant characteristic of the vector motion and that methods for its recognition may be useful in clinical diagnosis. But it is obvious that a more fundamental characteristic of vector behavior is the rotation of the spatial vector, and the question arises, to what extent does the apparent rotation in the frontal plane reflect the true motion of the vector in space. On consideration it will be seen that the true motion in space cannot be deduced from the apparent motion in the frontal plane. To make this fact obvious, let us assume that the spatial loop lies throughout its extent in one plane, that the generating point rotates continuously in one direction and that the frontal plane projection of the generating point appears to rotate clockwise. Now let the plane of the spatial loop be turned on an axis that lies within the plane and also passes through the origin, until the

*The terms sense of rotation and direction of rotation of the generating point or of the VC will be used interchangeably and with identical meaning. Clockwise rotation will be called positive; counterclockwise rotation will be called negative.

plane of the loop is perpendicular to the frontal plane. The projected loop will appear to become narrower, but without change in the sense of rotation, until the plane of the spatial loop reaches a position perpendicular to the frontal plane. As the turning is continued the projection in the frontal plane again appears as a loop, but the sense of rotation now will be counterclockwise. Hence we are forced to the conclusion that, if a slight change in the orientation of the spatial loop without other change in the character of the true vector motion causes the rotation of the VC to change from positive to negative, the sense of rotation in our constructed VC cannot be regarded as of certain and fundamental significance. There remains, however, the possibility that a study of the VC may show tendencies for changes in rotation to be correlated with states of the myocardium. Already it is apparent that in the normal heart the frontal projection of the QRS vector rotates clockwise in nearly all cases, while rotation in the opposite direction is common in cases of left ventricular hypertrophy or when there exists well-marked counterclockwise rotation of the heart on its longitudinal axis, such as is common in hearts occupying a transverse position.

When the cathode-ray apparatus is more generally available it is likely that the stereoscopic method will enable us to explore the meaning of the true motion of the spatial vector, but in the meantime there is an opportunity to search for provisional meanings in the constructed VC and thus to prepare for the more intimate study by more adequate means.

By methods which will be described it has been found practicable to recognize the sense of rotation of the generating point of the constructed VC with a fair degree of certainty in a considerable proportion of records. However, there is one type of record in which it is futile to attempt recognition. When a loop is very narrow and straight the curvature is too slight to permit recognition. This type of loop appears when the electrocardiogram shows in one lead a very slightly developed deflection, as in the approximately isoelectric T wave.

RECOGNITION OF SENSE OF ROTATION OF LOOP

The sense of rotation of the QRS loop usually can be recognized by mere inspection of the tracing. The loop almost always lies to some extent on both the positive and the negative sides of the x axis of one of the leads. In this case the electrocardiogram is diphasic in that lead and then the order of succession of the positive and negative phases of the deflection indicates the order in which the positive and negative halves of the vector field are traversed by the generating point (Fig. 6). The diphasic character most often is shown by the third lead tracing, but when no single lead gives a clear indication a decision often can be reached by taking account of a concurrent indication found in another lead.

In the case of the T loop, judgment is more difficult, for in the majority of records the T deflection is not diphasic in any lead. However, there are several special methods by one or more of which a conclusion usually can be reached. Three methods will be described; they will be arranged in the order of facility of application. Each of the methods, though sound in principle, may fail in certain cases. Usually it is best to employ more than one method and to accept the consensus.

First Method.—If the T wave is definitely diphasic in one or more leads, the sense of rotation can be recognized at once by application of the same principle as in the case of the diphasic QRS complex.

Second Method.—It may be seen by reference to any of the constructed VC's reproduced with this report that the generating point for either the QRS

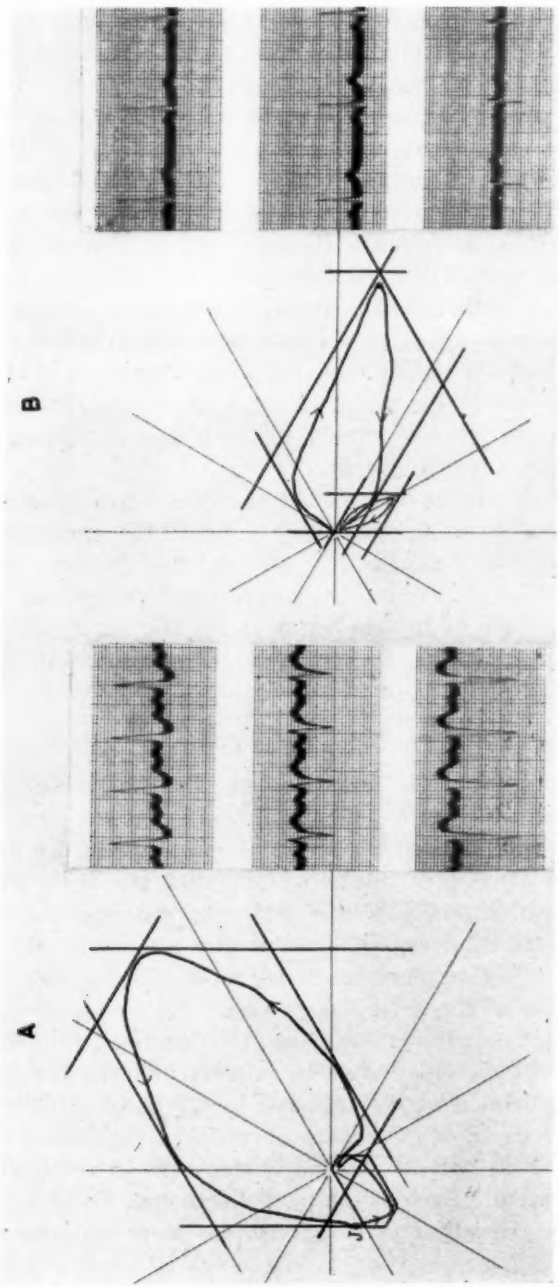

Fig. 6.—The two electrocardiograms, with their constructed VC's, are presented to illustrate the methods described in the text for determining the sense of rotation of the T loop. The scale for the QRS loop in *B* is reduced to one-half that employed for the T loop.

or the T loop, moving clockwise, reaches the positive boundaries of the enveloping polygon in the order: Lead I, Lead II, Lead III. If the rotation is counterclockwise this order is reversed. The modification of the rule for the case of maximum negative deflections is obvious. If then a T loop has been constructed from a particular electrocardiogram, the sense of rotation can be recognized if we learn the order in which the apices of the T waves were inscribed in two of the leads. In general, this can be determined by measuring the abscissas of the apices from simultaneous points in the two leads. In most records the apices of the R deflection, in the two leads where the R wave is highest, are very nearly simultaneous, the phase difference usually being less than 0.01 second (0.25 mm. with the usual recording speed). Consequently the apices of the R deflections usually may be taken as fairly reliable zero points for measuring the time interval to the apices of the T wave. But unless the phase difference of the two apices is found to be rather more than 0.25 mm., the significance of the measurement will be in some doubt and a conclusion as to which is the leading T wave should be made with some reserve. The conclusion can be tested by employing either the beginning or end of the QRS deflection as a base point, but these positions often are deceptive and their identification should be made with care after selecting complexes in which the breakaway point is clearly defined.

Third Method—The Curvature Test.—This test has proved to be very easily applied, requiring little more than mere inspection of the electrocardiogram. Unfortunately a somewhat involved explanation scarcely can be avoided if the principle is to be set forth adequately.

If the vector is turning clockwise, the slope of the VC continuously increases. This remains true in whatever quadrant the tangent to the VC may lie. If the slope is positive at the beginning of the loop it will assume increasing values until 90° is reached, where the value is infinite. As clockwise rotation is continued, the slope becomes negative but of large absolute value. Then smaller absolute values follow, but since they are negative they are, in fact, increasing. The same holds true throughout the full circle. Contrariwise, if the rotation is continuously counterclockwise the slope of the tangent diminishes continuously. If a function is increasing, its derivative is positive; if decreasing, its derivative is negative. Therefore we can learn whether dy/dx is increasing or diminishing at a given point on the curve by obtaining the derivative of that function and noting its sign. Since the function of which we seek the derivative is itself a derivative of y with respect to x, the result of the differentiation is the second derivative of y with respect to x. This will, as usual, be expressed by d^2y/dx^2. Therefore, to find the sign of d^2y/dx^2 for a particular point on the VC, we write the derivative of the right-hand member of each slope equation. From Equation 7 the derivative is

$$\frac{de_1 d^2e_2 - de_2 d^2e_1}{(de_1)^2} \qquad (7a)$$

From Equation 8 the derivative is

$$\frac{de_1 d^2e_3 - de_3 d^2e_1}{(de_1)^2} \qquad (8a)$$

inspection of the electrocardiogram. These relations are set forth in Fig. 5. The diagram provides data for a rough check on the correctness of the value of the slope obtained by measurements and calculation, but, more especially, it is useful for revising the original rough sketch of the VC.

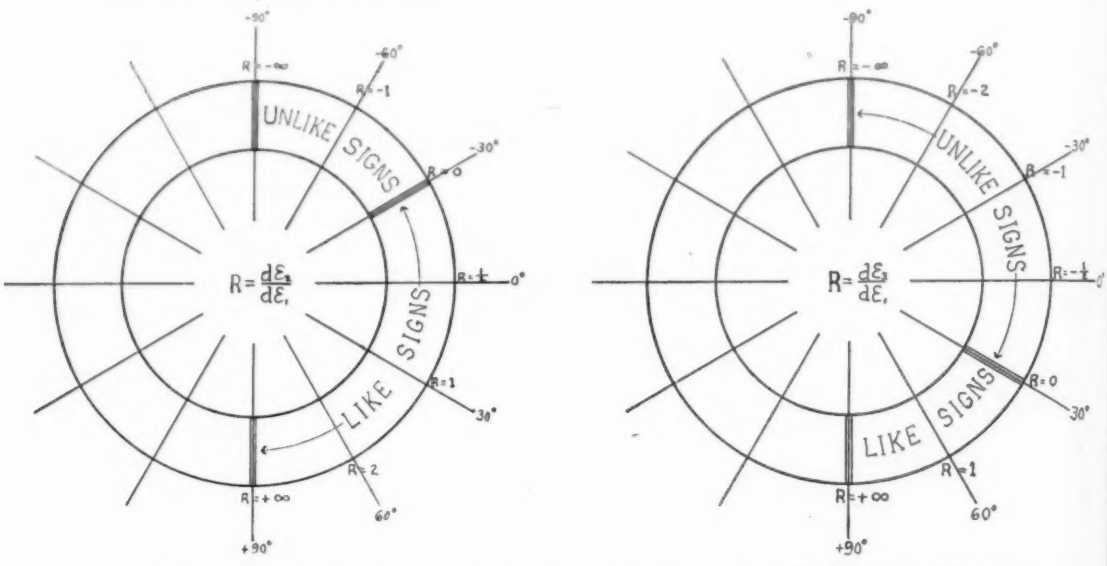

Fig. 5.—Diagrams for the rough estimation of the slope of a segment of the VC. The diagrams show the slope, dy/dx expressed as angle, of a segment of the VC when the ratio, de_2/de_1 or de_3/de_1, has the indicated value. The ratios of the slopes of the electrocardiographic tracings are represented by the symbol R. The corresponding slope of the VC is shown in one or the other indicated sector depending on the sign of the ratio. The value of R varies continuously from $-\infty$ to $+\infty$. For approximate results intermediate values of R may be interpolated visually. Use of the diagram may be illustrated as follows: if the slope of segment of the electrocardiogram in Lead II is about twice as great as the slope of the corresponding segment in Lead I the $R = 2$; if the slopes of the segments of the electrocardiogram are both positive or both negative, then the slope of the corresponding segment of the VC will be shown in the first diagram by the radius in the sector of like signs where $R = 2$. This slope is 60°. These diagrams must not be mistaken for representations of the vector field with the radii as vectors of electric force; the radii represent merely the slope of a segment of the VC, and the segment in question may lie in any part of the vector field.

THE ROTATION OF THE VECTOR

It seems probable that the sense of rotation of the VC* is a significant characteristic of the vector motion and that methods for its recognition may be useful in clinical diagnosis. But it is obvious that a more fundamental characteristic of vector behavior is the rotation of the spatial vector, and the question arises, to what extent does the apparent rotation in the frontal plane reflect the true motion of the vector in space. On consideration it will be seen that the true motion in space cannot be deduced from the apparent motion in the frontal plane. To make this fact obvious, let us assume that the spatial loop lies throughout its extent in one plane, that the generating point rotates continuously in one direction and that the frontal plane projection of the generating point appears to rotate clockwise. Now let the plane of the spatial loop be turned on an axis that lies within the plane and also passes through the origin, until the

*The terms sense of rotation and direction of rotation of the generating point or of the VC will be used interchangeably and with identical meaning. Clockwise rotation will be called positive; counterclockwise rotation will be called negative.

plane of the loop is perpendicular to the frontal plane. The projected loop will appear to become narrower, but without change in the sense of rotation, until the plane of the spatial loop reaches a position perpendicular to the frontal plane. As the turning is continued the projection in the frontal plane again appears as a loop, but the sense of rotation now will be counterclockwise. Hence we are forced to the conclusion that, if a slight change in the orientation of the spatial loop without other change in the character of the true vector motion causes the rotation of the VC to change from positive to negative, the sense of rotation in our constructed VC cannot be regarded as of certain and fundamental significance. There remains, however, the possibility that a study of the VC may show tendencies for changes in rotation to be correlated with states of the myocardium. Already it is apparent that in the normal heart the frontal projection of the QRS vector rotates clockwise in nearly all cases, while rotation in the opposite direction is common in cases of left ventricular hypertrophy or when there exists well-marked counterclockwise rotation of the heart on its longitudinal axis, such as is common in hearts occupying a transverse position.

When the cathode-ray apparatus is more generally available it is likely that the stereoscopic method will enable us to explore the meaning of the true motion of the spatial vector, but in the meantime there is an opportunity to search for provisional meanings in the constructed VC and thus to prepare for the more intimate study by more adequate means.

By methods which will be described it has been found practicable to recognize the sense of rotation of the generating point of the constructed VC with a fair degree of certainty in a considerable proportion of records. However, there is one type of record in which it is futile to attempt recognition. When a loop is very narrow and straight the curvature is too slight to permit recognition. This type of loop appears when the electrocardiogram shows in one lead a very slightly developed deflection, as in the approximately isoelectric T wave.

RECOGNITION OF SENSE OF ROTATION OF LOOP

The sense of rotation of the QRS loop usually can be recognized by mere inspection of the tracing. The loop almost always lies to some extent on both the positive and the negative sides of the x axis of one of the leads. In this case the electrocardiogram is diphasic in that lead and then the order of succession of the positive and negative phases of the deflection indicates the order in which the positive and negative halves of the vector field are traversed by the generating point (Fig. 6). The diphasic character most often is shown by the third lead tracing, but when no single lead gives a clear indication a decision often can be reached by taking account of a concurrent indication found in another lead.

In the case of the T loop, judgment is more difficult, for in the majority of records the T deflection is not diphasic in any lead. However, there are several special methods by one or more of which a conclusion usually can be reached. Three methods will be described; they will be arranged in the order of facility of application. Each of the methods, though sound in principle, may fail in certain cases. Usually it is best to employ more than one method and to accept the consensus.

First Method.—If the T wave is definitely diphasic in one or more leads, the sense of rotation can be recognized at once by application of the same principle as in the case of the diphasic QRS complex.

Second Method.—It may be seen by reference to any of the constructed VC's reproduced with this report that the generating point for either the QRS

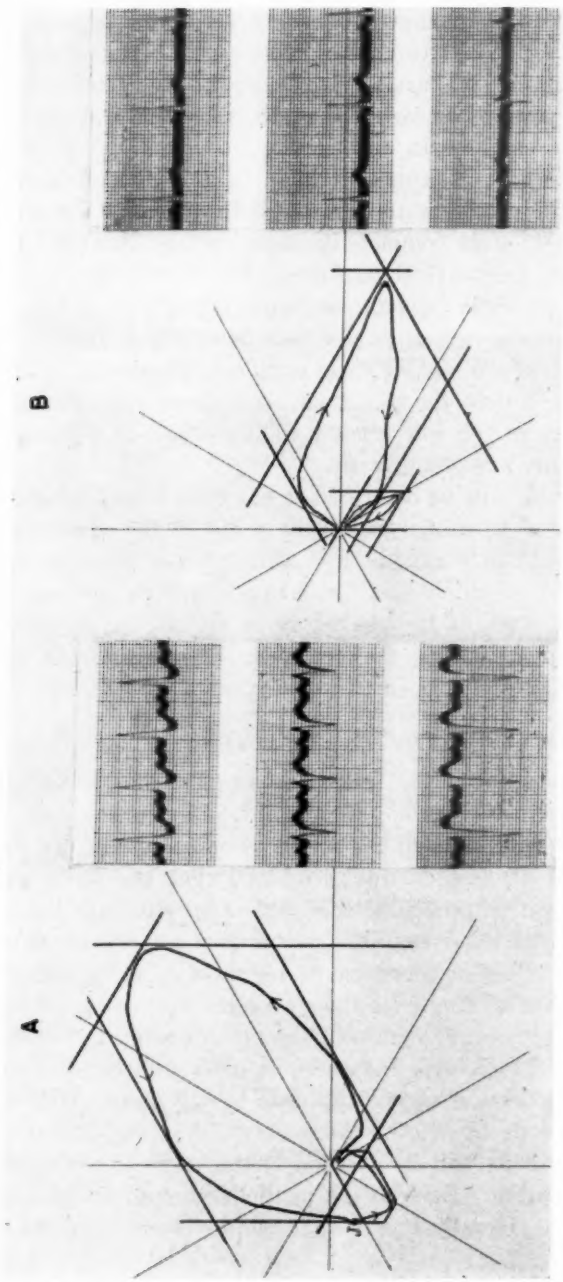

Fig. 6.—The two electrocardiograms, with their constructed VC's, are presented to illustrate the methods described in the text for determining the sense of rotation of the T loop. The scale for the QRS loop in *B* is reduced to one-half that employed for the T loop.

or the T loop, moving clockwise, reaches the positive boundaries of the enveloping polygon in the order: Lead I, Lead II, Lead III. If the rotation is counterclockwise this order is reversed. The modification of the rule for the case of maximum negative deflections is obvious. If then a T loop has been constructed from a particular electrocardiogram, the sense of rotation can be recognized if we learn the order in which the apices of the T waves were inscribed in two of the leads. In general, this can be determined by measuring the abscissas of the apices from simultaneous points in the two leads. In most records the apices of the R deflection, in the two leads where the R wave is highest, are very nearly simultaneous, the phase difference usually being less than 0.01 second (0.25 mm. with the usual recording speed). Consequently the apices of the R deflections usually may be taken as fairly reliable zero points for measuring the time interval to the apices of the T wave. But unless the phase difference of the two apices is found to be rather more than 0.25 mm., the significance of the measurement will be in some doubt and a conclusion as to which is the leading T wave should be made with some reserve. The conclusion can be tested by employing either the beginning or end of the QRS deflection as a base point, but these positions often are deceptive and their identification should be made with care after selecting complexes in which the breakaway point is clearly defined.

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From Equation 8 the derivative is

$$\frac{de_1 d^2e_3 - de_3 d^2e_1}{(de_1)^2} \qquad (8a)$$

From Equation 9 the derivative is

$$\frac{de_2d^2e_3 - de_3d^2e_2}{(de_2 - de_3)^2} \qquad (9a)$$

To determine whether the slope of the VC at a point is increasing or diminishing it is necessary only to know the *sign* of the second derivative. The sign of this function (Equations 7a, 8a, and 9a) is determined by the sign of the numerator in the parentheses, since the sign of the denominator in all cases must be positive. Now the sign of each term of the numerator can be recognized by mere inspection of the electrocardiogram. If the slope of the tracing is upward to the right, at the particular point selected for the test, de is positive, while a slope that is downward to the right makes de negative. If the slope runs horizontally de is zero. The terms d^2e_1 and d^2e_2 represent the rates of change of slope.* For our present purpose this function may be regarded as equivalent to "curvature." The sign of the curvature is positive if the tracing is concave upward and negative if convex upward. The sign of d^2y/dx^2 now may be determined by noting the sign of the slope and of the curvature at the chosen point in each of two electrocardiographic tracings, and combining the signs algebraically. In practice it is convenient first to write the significant numerator of Equation 7a, 8a, or 9a by substitution of symbols that have a more obvious meaning. Using S for slope and C for curvature these expressions then read:

for Lead I and Lead II,	$S_1C_2 - S_2C_1$
for Lead I and Lead III,	$S_1C_3 - S_3C_1$
for Lead II and Lead III,	$S_2C_3 - S_3C_2$

These expressions will be referred to as the "curvature formulas." They are not the exact mathematical equivalents of the numerators in the parentheses in Equations 7a, 8a, and 9a, but, as previously explained, they serve as guides for combining the signs of the slopes and of the curvatures, resulting in a correct determination of the sign of the second derivative. The formulas are to be used in the following manner: Having selected corresponding short segments of the T wave in, say, Leads I and II, the signs of the slopes and curvatures are noted and written down in place of the symbols in the first of the curvature formulas. For example, in the electrocardiogram of Fig. 6, *A*, at a point about the middle of the S-T segment in Lead I both the slope and the curvature are positive, while in Lead II in the corresponding segment the slope is positive and the curvature is negative. Thus the signs, as written down, read (+−) − (++). In this case the sign of the whole expression is negative and the slope of the corresponding segment of the VC is shown to be diminishing, that is, the T loop is being traced counterclockwise.

*The rate of change of slope, sometimes called the "flexion" of the curve, is related to, but is not identical with, curvature. For an exact statement of the relation a textbook on calculus should be consulted. For the purpose of the present analysis it is sufficient to state two facts concerning the relation. First, the flexion (d^2e) and the curvature always have the some sign. Second, if the slopes are equal in two curves, the flexions are proportional to the curvatures. For these reasons, in the use of the change of slope equations, no error will be introduced by assuming that the d^2e terms actually stand for curvature.

The availability of this procedure unfortunately is limited to a considerable extent by the fact that, if both terms of the formula are positive or both are negative, the resultant sign remains indeterminate without a knowledge of the absolute values of the S and C quantities, for, under this condition, the sign of the difference will depend on which term is the larger, and this we have no simple means of determining. However, there is one condition, easily recognized, under which this difficulty does not arise, and the success of the test is assured, namely, when the two slopes are of the same sign and the two curvatures are of opposite signs, or vice versa. In this case the two terms of the formula will have unlike signs and the relative magnitudes will not affect the sign of the difference.

There are two special cases, frequently occurring, in which the curvature formula may be applied with great ease. (A) If a point of zero slope can be found in one lead while at the corresponding point in the other lead the slope is not zero, then the formula reduces to one term and the sign of the whole expression is evident. This test readily may be employed in the analysis of the tracing in Fig. 6, *A*, where T_2 has zero slope at the point of maximum deflection while at the corresponding point in T_1 the slope is positive. In this case the formula, written with signs only, reads $(+-) - (0+)$. The whole expression, then, has a negative sign, thus indicating a counterclockwise rotation of the VC. (B) As explained in the footnote on page 206, the magnitude of two curvatures properly may be compared when the slopes are equal. Hence we have the following rule: If a segment in one lead has a curvature sensibly greater than the curvature in the other lead, and, if in the corresponding segments the tracing of greater curvature has a slope at first less, and then greater, than in the other lead, it is obvious that at some point in the region of curvature the slopes will be equal. It is not necessary that this point be identified; the knowledge that it exists is sufficient. Since the greater of the C terms is known by inspection of the tracings and the S terms are equal at some point in the segment in question, the greater of the two terms of the curvature formula is obvious and the sign of the whole is readily found. Electrocardiograms in which this procedure is applicable are of frequent occurrence, and a record of this type is shown in Fig. 6, *B*. If points near the middle of the S-T segments of Lead I and Lead II of that record are examined it readily can be seen that at some point the slopes are equal and positive and that the curvature at that point in Lead II is greater than in Lead I, and that in each lead the curvature is positive. Hence $S_1C_2 > S_2C_1$ and the sign of the whole expression is positive. Therefore, the T loop in the segment in question is rotating in a clockwise direction.

The curvature test, of course, reveals the sense of rotation only of the limited segment to which it is applied, but usually it is true that the rotation obtaining in any considerable segment of the T loop will be found to prevail throughout. If T loops in the form of lunes, figures of eight or other more complicated figures were common, the determination of the direction of rotation at one, or even at two points could not be trusted, but such forms appear to be uncommon. Through the kindness of Dr. Mann I had an opportunity to search through a large number of his recorded monocardiograms and failed to find an instance of a deceptively irregular loop; in all cases where the loops

were clearly inscribed they appeared as somewhat irregular ellipses each having a rotation, the sense of which was maintained throughout. It is desirable that this point be verified by means of VC's electrically recorded and made with reduced light intensity so that the form of the T loop may be recorded clearly throughout its full path.

THE VELOCITY OF INSCRIPTION IN A SEGMENT OF THE VECTORCARDIOGRAM

The electrocardiogram is a time-potential graph, but the process by which the VC is constructed eliminates the time factor from the result; therefore the time required for the generating point to trace out any given segment cannot be determined without a further analysis. In the case of the electrically recorded VC Wilson revealed the velocity of inscription by the ingenious device of interrupting the accelerating voltage through the cathode-ray tube at a known frequency, say two hundred interruptions per second. The effect of this was to make the tracing appear as a series of dashes the number of which per unit length of the curve indicated the velocity. It has seemed desirable to introduce the velocity characteristic into the constructed VC, and a practicable means to this end will be described.

The velocity of inscription in a chosen segment may be determined rather simply by the use of the following principle. If at any point in the VC the rate of increase of the distance of the generating point from the x_1 axis is known, and if the direction of motion of the generating point at that instant also is known, the linear velocity of inscription may be represented by the equation

$$ds = \frac{dx}{\cos \theta} \qquad (10)$$

where ds stands for the linear velocity, dx for the horizontal component of that velocity, and θ for the angle between the horizontal and the tangent to the VC at the point in question. dx is essentially identical with the de_1 of Equations 7, 8, and 9, that is, it is the slope of the electrocardiogram in the corresponding segment. Heretofore, the slope of the electrocardiographic tracing has been expressed as angle or tangent of angle, but for the present purpose it conveniently may be expressed as millivolts per second. Unit slope may be taken as 45°, where the tangent is unity, and at this angle the rate of change of slope is 2.5 mv per second. Therefore, when the slope of the electrocardiogram at a chosen point in Lead I has been determined, the horizontal component, dx, of velocity may be found by multiplying 2.5 mv per second by the measured electrocardiographic slope. Then, to find $\cos \theta$, three steps are taken: (1) de_2 or de_3 is found by the use of the protractor and tables; (2) dy/dx, the slope of the VC in the corresponding segment is found by means of Equation 7, 8, or 9; and (3) the cosine of the angle represented by dy/dx is found in tables. With dx and $\cos \theta$ known, ds is found by substitution in the velocity equation (10). The measurements and calculations readily can be made in a few minutes, but, after a little practice, rough results may be obtained by means of visual estimates of the rate of change of voltage in the first lead and of the slope of the selected segment of the VC. When this method (with measurement and calculation)

was applied to the electrocardiogram and VC of Case 1 of Fig. 8 the rate of inscription of the excursion was found to be 9.1 mv per second while the velocity calculated directly from the recorded VC was 8.1 mv per second. The rate of recursion, determined by the method of this paper, was 4.9 mv. per second, while calculated directly from the recorded VC the rate was 4.1 mv per second. The correspondence of these results is close enough to indicate that the method may be useful for some purposes.

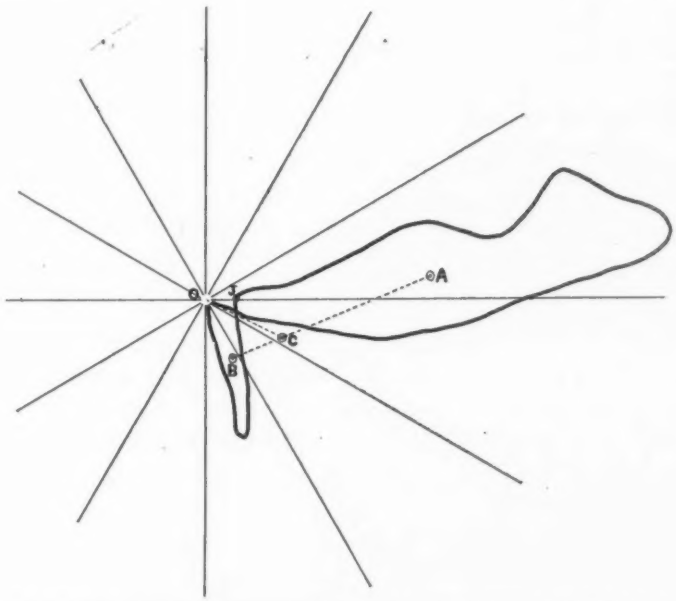


Fig. 7.—Calculation of the common center of gravity of QRS and T loops. The diagram represents a hypothetical case. The estimated center of gravity of QRS is at *A*, and that of T is at *B*. The assumed duration of QRS is 0.10 second, that of T is 0.30 second, and that of QRS-T is 0.40 second. The center of gravity of QRS-T is at some point *C* on the line *AB*. To locate *C* the calculation is as follows: $AC \times 0.10\ (second) = CB \times 0.30\ (second)$; $AC = 3\ CB$; $AC = 3\ (AB - AC) = \frac{3}{4}\ AB$; *AB* measures 5.8 cm., therefore $AC = 4.35$ cm. *C* being the center of gravity the line *OC* is the mean vector of QRS-T. The length of *OC* is 2.3 centimeters. Since 1 cm. represents 100 μv, the magnitude of the mean vector, or of the potential gradient, is 230 μv, and the time-potential gradient (Wilson's gradient) is 230×0.4 second or 92 μv per second. The direction of the gradient is 26°.

THE RELATION OF THE VENTRICULAR GRADIENT TO THE VECTORCARDIOGRAM

Wilson and his co-workers[12, 13] derived the concept of the ventricular gradient directly from the electrocardiogram but it also is possible to define the gradient in its relation to the VC. A brief statement of this relation will be made here. Some may find the concept more readily grasped if it is stated graphically in VC terms. Moreover, the argument will show that a rough approximation to the gradient may be made by mere inspection of the VC, and it is possible that such an estimate, although crude, may be of use in the practical application of gradient data in clinical medicine.

The ventricular gradient, as Wilson described it, is a vector having the direction of the mean electrical axis of the QRS-T period and a magnitude equal to the product of the mean manifest potential by the duration of the QRS-T

period. It is evident then that the magnitude of the ventricular gradient is a quantity having the dimensions of both voltage and time. This product is equal to the *manifest area* of QRS-T. It will be shown in the present discussion that it is possible to determine, directly from the VC, a vector having the direction of the mean electrical axis and a magnitude equal to the mean manifest potential unmodified by a time factor. This vector magnitude has only the dimension of voltage. It will be convenient for the purposes of this discussion to call the vector derived from the VC the *potential gradient* and to refer to the gradient calculated as described by Wilson as the *potential-time gradient.* Obviously the latter may be derived from the former by multiplying by the time duration of the QRS-T.

The following symbols with the stated meaning will be used in what follows.

E_m, a vector having the magnitude of the manifest potential and the direction given by the Einthoven equation, $e = E_m \cos \alpha$. The symbol sometimes may be interpreted as a magnitude without reference to direction.

$\overline{E}_m$, the mean vector of the infinite series of vectors, each equal to E_m throughout an interval (QRS, T, or QRS-T).

t, the duration of a time interval.

The possibility of deriving the potential gradient from the VC depends on the identity of the manifest potential, E_m, of the electrocardiogram and the generating vector of the VC, and the consequent identity of the mean vector, $\overline{E}_m$, for both curves. Since this matter is not one to *sauter aux yeux* a brief explanation may be helpful.

If it were technically possible to record the manifest potential differences (magnitude of E_m) instead of merely the components thereof, the tracing produced might appropriately be called the *manifest QRS-T.* The area under this curve would be the *manifest area* of QRS-T. The manifest QRS-T may be thought of as traced by the upper end of a vertical line, or ordinate, standing on the base line, representing by its length the varying magnitude of the manifest potential, E_m, and advancing at a constant rate by short equal steps, of length Δt. The mean ordinate of this curve obviously is the mean value of the manifest potential, that is, $\overline{E}_m$.

Turning now to the VC, we may picture it as traced by the terminus of a line which, like the ordinate of the manifest QRS-T, is equal in length to the manifest potential at every instant throughout the QRS-T period. But, unlike the vertical, evenly progressing, ordinate of the manifest QRS-T, the foot of the VC vector is fixed at the origin while the terminus sweeps through the field describing an arc to form a complete loop.

Both the vector of the VC and the ordinate of the manifest QRS-T represent the same electrical quantity, the manifest potential. They are essentially identical, except that the VC vector has direction as well as magnitude, whereas the ordinate has magnitude only, the varying direction of the electric force of which it is an expression being implicit in the ratio of the component voltages in two leads.

The analytical expression for the *mean manifest potential* is

$$\bar{E}_m = \frac{1}{t}\int_o^t E_m dt \qquad (11)$$

This equation serves equally well to express the mean magnitude both of the ordinate of the manifest QRS-T and of the vector of the VC. The meaning of the equation, as it applies to the manifest QRS-T, may be clearer if it is pointed out that the integral, without division by time, is the magnitude of the area under the manifest QRS-T, that is the *manifest area.* If this manifest area is represented by an equivalent rectangle constructed on the base line under the manifest QRS-T it is evident that the height of the rectangle will be equal to the mean ordinate of the curve. The height of the rectangle is found by dividing the area by the length of the base, that is by the time. It is for this reason that the integral (manifest area) in the above equation is divided by t to give the value of the mean ordinate $\bar{E}_m$.

The application of the equation to the case of the VC is not quite so evident, since time is not shown explicitly in the VC. It therefore is desirable to replace dt by an element of arc, ds, provided the relation of ds to dt is known. This relation and the consequences of the substitution will be shown in what follows.

It at first will be assumed that the velocity of inscription of the VC is constant. The assumption does not greatly exceed the possibility, for an electrocardiogram in which the up and down strokes of QRS are approximately straight lines and form symmetrical peaks in both leads yields a QRS loop in which the velocity is nearly constant. If the velocity is constant then equal lengths of arc represent equal time intervals and the differential ds, representing an element of arc, may be substituted for dt, a corresponding change being made in the limits of integration and in the coefficient. When these substitutions are made Equation 11 becomes

$$\bar{E}_m = \frac{1}{s}\int_o^s E_m ds \qquad (12)$$

The co-ordinates of the terminus of the mean vector $\bar{E}_m$, are given by the equations

$$\bar{x} = \frac{1}{s}\int_o^s x ds \quad \text{and} \quad \bar{y} = \frac{1}{s}\int_o^s y ds$$

These latter are the familiar equations for the centroid of a curve. Thus, the mean vector of a VC loop, if the latter is inscribed with constant velocity, can be constructed by drawing a straight line from the origin to the centroid of the loop.

The assumption of constant velocity now will be dropped and the influence of variable velocity examined. If a segment of the VC is slowly inscribed the vectors to that segment, spaced at equal time intervals, will be numerous and will "weight" the mean value of the vectors. Where the vectors are close set the amount of time in a unit length of the VC will be large. In the VC, time

may be considered as analogous to mass in the case of a thin wire formed in a loop, and it has the same effect on the center of gravity, i.e., slowness of inscription in one segment will cause a displacement of the center of gravity toward the segment. Carrying the analogy further and remembering that the density of a wire is the mass per unit length, we may coin the expression *time density* for use with the VC, and define the term as the amount of time in a unit length of the VC. If ρ represents time density, $\rho = \frac{dt}{ds}$ or $dt = \rho ds$. Evidently ρ is the reciprocal of the velocity.

If, now, the differential, dt in Equation 11, is replaced by ρds, we obtain the equation for the mean vector of a VC of variable velocity.

$$\bar{E}_m = \frac{\int_0^s \rho E_m ds}{\int_0^s \rho ds} \qquad (13)$$

Corresponding equations for the co-ordinates of the terminus of the mean vector readily may be written, and these will be also the equations for the co-ordinates of the center of gravity of the loop. It is apparent then that the terminus of the mean vector of a VC loop is at the center of gravity of the loop, whether the velocity of inscription is constant or variable.

With these relations in mind, a rule now may be formulated for an approximate method of locating the center of gravity of a VC loop and thereby determining the mean vector, or the potential gradient. By inspection locate and mark the center of gravity of the loop considered as if it were of uniform time density, allowing due weight for the large moment of portions of an irregular curve that project far out from the general region included by the curve, and for the lesser moment of re-entrant portions of the curve. Then roughly estimate the relative velocity in the several parts of the curve, using the velocity equation (Equation 10) mentally applied. Crosshatch the curve with close set lines to indicate slow inscription and with widely spaced lines in regions of high velocity. The cross hatching serves to indicate the estimated variations in the time density. Then choose a point removed from the geometrical centroid in a direction and for a distance which allows for the "weight" of regions of slow velocity and for the "lightness" of regions of high velocity. The center of gravity is shifted toward "heavy" regions, away from "lighter" regions. But it should be remembered that the principle of the lever is involved in center of gravity dynamics; consequently the influence of weight of segment varies with the distance from the center of gravity. A more exact statement of the dynamic principles involved is given in an appendix.*

*The reader readily may test his ability to make fair estimates of the center of gravity of VC loops in the following way. Shape a piece of copper wire to form an irregular loop in one plane. Draw the outline of this loop on paper and mark a point which is estimated to be at the center of gravity. Now slip a thread, held taut, under the wire and move the thread until, when it is lifted slightly, the loop is found to be in balance. Mark the position of the thread and draw a line to show the position. Repeat this operation with the thread crossing the loop at a considerable angle from its first direction. Draw a line to show this second balance position of the thread. The intersection of the two lines is at the center of gravity of the loop. This test, when made by a number of people, revealed a considerable innate capacity for making a good estimate.

Having located the center of gravity of both the QRS and the T loops, the center of gravity of the whole VC is to be found. Here, again, time plays the role of mass. The duration, or mass, of QRS and that of T may be considered as concentrated at the respective centers of gravity of the loops. The common center of gravity (Fig. 7) lies on a connecting line AB at a point C that subdivides AB according to the equality of moment arms principle, that is, so that

$$Mass_A \times AC = Mass_B \times CB$$

For practical use this equation may be transformed to give AC in terms of quantities readily measured on the electrocardiogram and VC. Thus we have

$$AC = \frac{T\ interval}{QRS\text{-}T\ interval} \times AB$$

A line drawn from the center of the field to the point C is the mean vector of the whole ventricular complex, or the potential gradient. It may be measured by means of a scale to give the magnitude of the gradient and, by means of a protractor, for the direction.

Those who have taken the pains needed to make accurate determinations of ventricular gradients by Wilson's method of area measurements on the electrocardiogram may be skeptical of the reliability of gradient estimates based on intuitive judgments of this sort but, on trial, results were obtained which suggest that the method may be useful for some purposes. These results are illustrated in Fig. 8 and tabulated in Table I.

TABLE I. THE POTENTIAL-TIME GRADIENT DETERMINED FROM ESTIMATE OF THE CENTROID OF THE QRS LOOP OF THE CONSTRUCTED VC AND COMPARED WITH THE SAME FUNCTION DETERMINED BY WILSON'S METHOD OF AREA MEASUREMENTS

	FROM ESTIMATE OF CENTROID OF QRS LOOP OF VC		FROM AREA MEASUREMENTS OF QRS IN ELECTROCARDIOGRAM	
CASE	MAGNITUDE IN μV/SEC.	ANGLE	MAGNITUDE IN μV/SEC.	ANGLE
1	84	- 41°	84	- 36°
2	174	- 56°	186	- 64°
3	164	- 44°	140	- 52°
4	25	- 42°	42	- 33°
5	92	-172°	83	-147°
6	70	- 83°	68	- 83°

For graphic representation of these quantities see Fig. 8.

The electrocardiograms and the recorded VC's are reproduced from records of six cases published by Wilson and Johnston,[1] who kindly furnished me with photographic copies of the records. The constructed VC's were drawn from the electrocardiograms without the recorded VC's being in view or in mind. Drawn several years ago at the beginning of these studies they represent the approximations to the true VC which may be made by a novice. The gradient determinations were made recently and without any previous experience in estimating this function. In this test only the QRS period was dealt with; presumably the results would have been about as good if the whole QRS-T period had been covered.

The units in which the magnitude of the voltage gradient is expressed may be chosen at will, but the microvolt, used by Wilson, is well suited for the measurement of the mean vector as derived from the VC. The field described

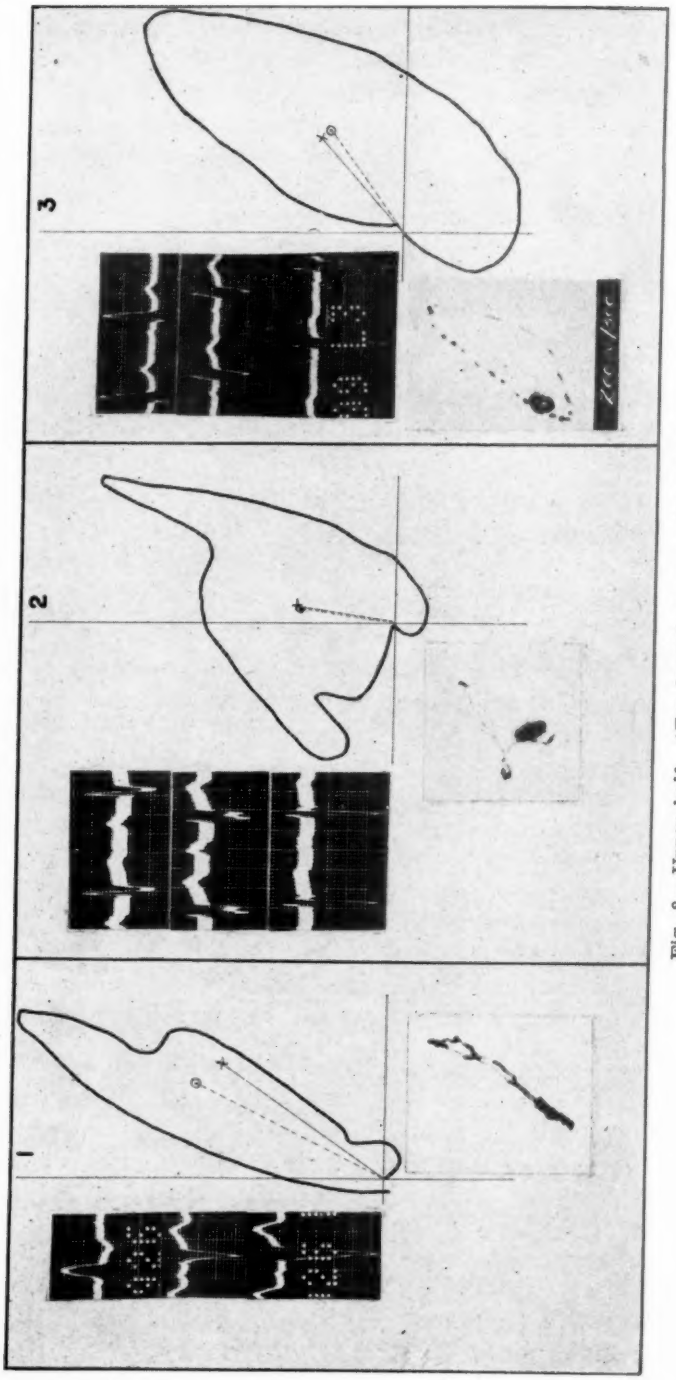
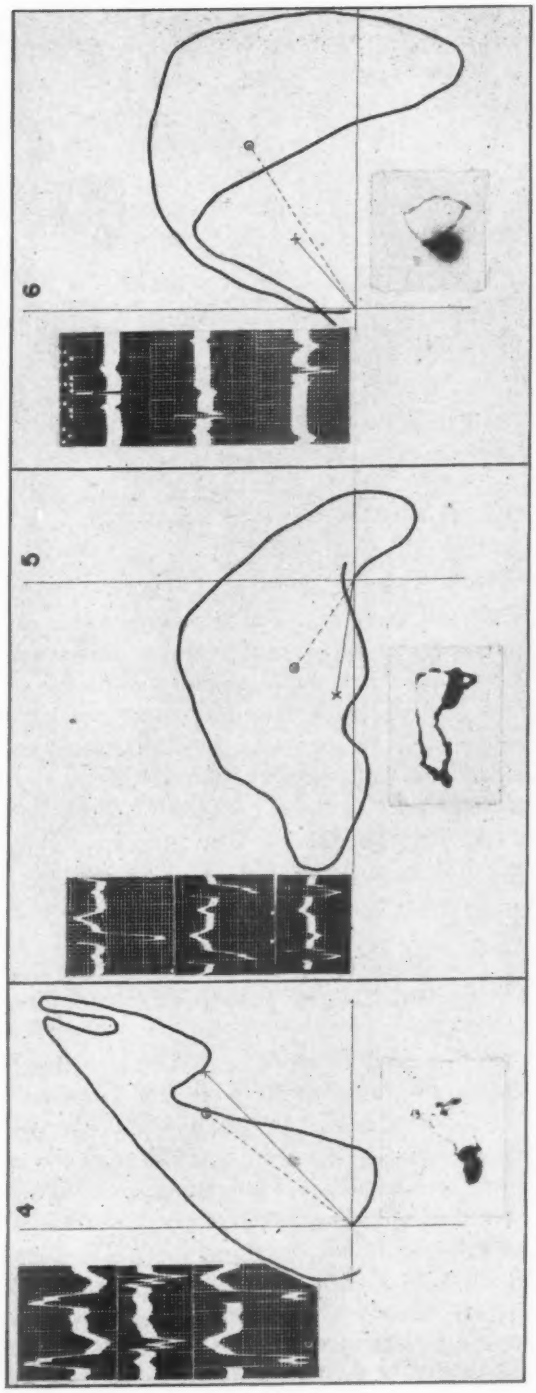


Fig. 8.—Upper half. (*For legend see opposite page.*)



Lower half.

Fig. 8.—Constructed VC's of six cases are shown, with the electrocardiograms and the VC's recorded by Wilson. In each constructed VC the estimated mean vector is shown as a broken line from the origin to a point marked by a small circle. The mean vector determined by the method of measured areas is shown as a continuous line ending in a small x. The estimation of the mean vector in the VC's in the lower row is less satisfactory, the errors being due chiefly to avoidable faults in sketching the VC or in estimating the relative velocity of inscription in certain segments. Some of these faults are obvious and may be more instructive than if the execution were faultless. For numerical data see Table I.

early in this paper is so constructed that 1 cm. along any radius represents 0.1 mv or 100 μv potential difference in that direction. If it is desired to transform the magnitude of the potential gradient to a quantity identical with the potential-time gradient of Wilson it is necessary only to multiply the magnitude of the potential gradient by the duration of the QRS-T interval expressed as a fraction of a second.

CONCLUSIONS

The vectorcardiogram is of value, first of all, because it exhibits the behavior of the heart's electric vector simply and realistically. Wilson and Johnston[1] in their paper on the recorded vectorcardiogram, observed that, for teaching purposes, "It makes it possible to visualize the electromotive force of the heart as a single natural entity unobscured by the artificialities and complexities introduced by splitting it into a system of components in the arbitrary frame of reference defined by the standard leads." But if the unitary and simple character of the VC aids the beginner to grasp more clearly the course of electrical events in the heart it is not, perhaps, extravagant to say that all who attempt interpretation of the electrocardiogram likewise would derive from the VC clearer views of the electrical events and thus might more surely arrive at true meanings. Electrocardiography has become cluttered by a mass of detail, a consequence of dealing with a threefold complex of components instead of the single entity expressed by the components. The remedy for this particularism is the recognition of elementary characteristics of vector behavior and a diligent study of correlations between these prime features and known cardiac processes and states. The grammar of the electrocardiogram cannot yet be written, but to illustrate the thought expressed here several basic characteristics of the VC may be mentioned—the magnitude and the direction of the major axes of the two VC loops, the angle of divergence of the two loops, the direction of rotation, the ratio of the major and minor axes of the loops, and the direction and amount of displacement of *J*. In addition there should be mentioned the ventricular gradient, the early studies of which already give promise of utility. If electrocardiography is to progress and if it is to be intelligible to those whose varied interests preclude specialization, then it seems to be imperative that the threefold Einthoven record be integrated to make possible clear concepts and simple descriptions.

In a later paper I hope to report on a study now in progress on the basis of which a number of electrocardiographic patterns will be discussed in the light of the VC representation. However, one of the observations already made may be stated here to illustrate how the VC possibly may extend the range of information derived from the electrocardiogram. On examining the sense of rotation of the QRS loop in the records of about fifty presumably normal individuals a positive (clockwise) rotation was found in all but two or three. Moreover the rotation of T also was found to be positive. On the other hand, in a group of cases with left axis deviation, but without other evidence of abnormality, the rotation of the QRS loop was negative. In these the rotation of T also was negative. But in still another group showing left axis deviation, together with well-marked clinical evidence of myocardial disease, the rotation of the QRS loop was positive, while that of T was negative. These observations are

not yet extensive enough, nor made in sufficient detail, to warrant a firm conclusion, but it seems likely that, when the heart is normal and in the average normal position in the chest, the rotation of the QRS loop always is positive, with positive rotation of T; that, as left axis deviation develops, the inclination of the plane of the spatial vector motion changes so that, in the frontal plane, the rotation of QRS appears negative; but that, if the myocardium then becomes seriously diseased, the rotation of the leftwardly deviated QRS loop is reversed, becoming positive again, while the rotation of T remains negative and opposed to that of QRS. If further studies confirm this apparent influence of myocardial disease on the sense of rotation of the loops and on the concordance of rotation in the two loops, then the VC representation can be said to have revealed a sign of disease which is implicit, but not apparent, in the electrocardiogram.

In Aristotelian metaphysics it was taught that the result of a synthesis is a new entity, not merely the sum of the parts. The truth of this aphorism is exemplified in many fields of science. Appositely, the VC may be viewed as an entity having a capacity for usefulness beyond that of the electrocardiogram from which it is derived. The technique of VC construction described in this paper provides a means by which the worker in electrocardiography readily may explore this possibility without the need of apparatus of any sort.

APPENDIX

The Center of Gravity of a Loop of Varied Velocity.—As stated earlier in this paper, it is possible to make a fair estimate of the approximate position of the center of gravity of the VC by mere inspection of the curve. But a judgment of this sort is more likely to be good if there is understanding of the dynamic principles involved. The following analysis of a simplified, but pertinent, center of gravity problem should be helpful to such an understanding. But the method used, although exact in principle, scarcely can be applied exactly to an actual VC. The problem and its solution are presented merely as an aid to intuitive judgment.

The half cardioid *ODEF* (Fig. 9) and the half loop of a "four leaf rose" *FGO* are joined to represent an asymmetrical QRS loop. For measurements, the intercept on the x axis is taken as unity. The centroid of *ODEF* is at A ($\bar{x} = 0.4$, $\bar{y} = 0.4$), that of *FGO* is at B ($\bar{x} = 0.518$, $\bar{y} = -0.175$). The ratio of the length of *ODEF* to that of *FGO* is 2:1.25. Assuming that a line has density and that the loop is of uniform density the masses of the two curves are respectively proportional to their lengths. Indicating the mass of the cardioid portion of the loop by M_c and that of the rose portion by M_r we have

$$\frac{M_r}{M_c} = \frac{1.25}{2.00}$$

For the purpose of dynamic analysis the whole mass of a line may be considered as concentrated at its centroid. Hence the center of gravity C of the loop is identical with the center of gravity of the two masses concentrated at A and at B, respectively. The location of C is to be found by employing the principle of equality of moment arms. Thus

$$M_c \times AC = M_r \times CB \text{ or } \frac{AC}{CB} = \frac{M_r}{M_c} = \frac{1.25}{2.00}$$

If the velocity in one segment of the loop is varied the center of gravity will be displaced, provided the concept of "time density" (time per unit of length) is substituted for the usual concept of density (mass per unit of length). The time density is the reciprocal of the velocity and will be represented by ρ. If the time density in a segment is increased, the center of gravity will be displaced toward this segment; a decrease in the time density will cause a displacement in the opposite direction.

To define this effect more exactly the loop now will be supposed to have uniform velocity except in the segment to the left of the y axis, where a different, but uniform, velocity obtains. P is the center of gravity of this segment, with co-ordinates, $\bar{x} = -0.83$, $\bar{y} = 0.242$. It is desired to calculate the displacement of the center of gravity from the point C caused by the variation of time density in the segment. If the time density in the varied segment is n times the unit density prevailing in the rest of the loop the variation of time density will be $n\rho - \rho$

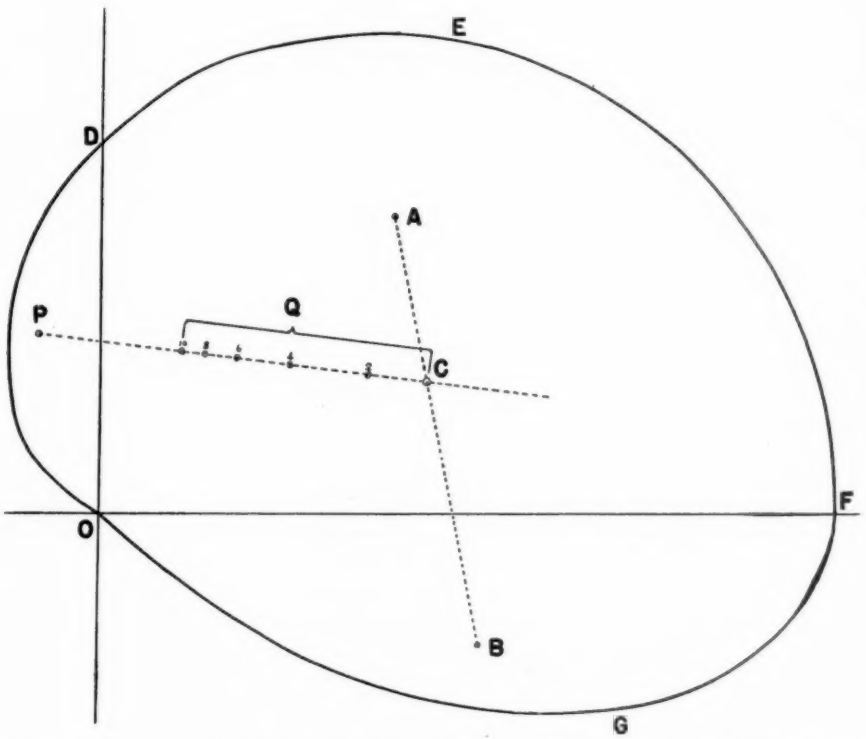


Fig. 9.—Conventionalized QRS loop formed by joining the half cardioid *ODEF* (Qr = Cos θ + 1), to half of one leaf of a "four leaf rose" *FGO* (r = Cos 2 θ). The intercept on the x axis is taken as unity. Length of half cardioid = 2; length of half rose leaf = 1.25; length of segment to left of y axis = 0.586; *A* is at centroid of half cardioid ($x = 0.4$, $y = 0.4$); *B* is at centroid of half rose leaf ($x = 0.518$, $y = -0.175$); *C* is at centroid of combined curve ($x = 0.446$, $y = 0.179$); *P* is at centroid of segment to left of y axis ($x = -0.083$, $y = 0.242$); *Q* indicates variable location of center of gravity of the whole loop dependent on the "time density" of the segment to left of the y axis; numerals indicate the respective locations of the center of gravity of the whole loop, with the time density varying from 1 to 10.

or $(n - 1)\rho$. The variation of mass of the segment is given by the product of the time density by the length (l) of the segment, that is, it is $(n - 1)\rho l$. If this amount of mass is considered to be concentrated at P, the centroid of the segment, while the mass of the whole loop of uniform density is concentrated at C, then the new center of gravity Q may be found by application of the principle of equality of moment arms. If the mass of the whole loop of uniform time density is expressed by ρL (where L is the whole length of the loop) then we may write the equation

$$CQ \times \rho L = QP \times (n - 1)\rho l$$

$$\text{or } \frac{CQ}{QP} = \frac{(n - 1)\rho l}{\rho L}$$

If the length l of the segment is expressed as a fraction of the total length, L, of the loop, the last equation may be written

$$\frac{CQ}{CP} = \frac{(n - 1)l}{(n - 1)l + 1}$$

The idea expressed by this last equation may be shown in another and simpler form if the symbol ΔM_s is used for the variation of mass of the segment. Thus percentage displacement

$$\text{of } Q \text{ toward } P = \frac{\Delta M_s}{\Delta M_s + 1} \qquad (14)$$

If the velocity of inscription in the varied segment is greater than in the rest of the loop n is negative and the displacement of the center of gravity is to be measured on the extension of PC away from the segment.

Returning to the diagram of Fig. 8 we may, by way of illustration, calculate the displacement of the center of gravity on the assumption that the velocity of inscription of the segment is one-fourth as great as in the rest of the loop. In this case the time density is fourfold and $n = 4$. The variation of density, $n - 1$, is 3. The length of the whole loop is 3.25, while that of the segment is 0.59, making the relative length of the segment 0.18. Thus the variation of mass, $(n - 1)l$, is 0.54. Then by Equation 14 we have

$$\frac{CQ}{CP} = \frac{0.54}{1.54} = 0.35$$

We conclude that the fourfold slowing of inscription of the segment causes displacement of the center of gravity from its position at C to a point, Q, about one-third of the distance toward P.

In the diagram the points along the line, CP, represent the several positions of the center of gravity when the time density of the segment has the several values shown by the adjacent numerals.

REFERENCES

1. Wilson, Frank N., and Johnston, Franklin D.: The Vectorcardiogram, AM. HEART J. 16: 14, 1938.
2. Schellong, F., Heller, S., and Schwingel, E.: Das Vektordiagramm; eine Untersuchungsmethode des Herzens, Ztschr. f. Kreislaufforsch. 29: 497, 1937.
3. Schellong, F., and Schwingel, E.: Das Vectordiagramm; eine Untersuchungsmethode des Herzens; über die Bedeutung von Knotungen und Aufsplitterung in QRS des Ekg, Ztschr. f. Kreislaufforsch. 29: 596, 1937.
4. Schellong, F., Schwingel, E., and Hermann, G.: Die praktisch-klinische Methode der Vektordiagraphie und das normale Vektordiagramm, Arch. f. Kreislaufforsch. 2: 1, 1937.
5. Schellong, F.: Grundzüge einer klinischen Vektordiagraphie des Herzens, Ergebn. d. inn. Med. u. Kinderh. 56: 657, 1939.
6. Hollmann, W., and Hollmann, H. E.: Neue elektrokardiographische Untersuchungsmethoden. II. Die dreiphasische Vektordarstellung der Potentialresultanten des Herzens, Ztschr. f. Kreislaufforsch. 29: 546, 1937.
7. Hollmann, H. E., and Hollmann, W.: Das Einthovensche Dreiecksschema als Grundlage neuer elektrokardiographischer Registriermethoden, Ztschr. f. klin. Med. 134: 732, 1938.
8. Hollmann, H. E., and Hollmann, W.: Das Einthovensche Dreiecksschema im Vergleich zu anderen Ableitungsschemen, Arch. f. Kreislaufforsch. 3: 191, 1938.
9. Hollmann, W., and Guckes, E.: Das Triogramm und seine klinische Bedeutung, Arch. f. Kreislaufforsch. 4: 69, 1939.
10. Guckes, Ernst: Zur Technik der zwei- und dreiphasigen Darstellung des menschlichen Herzvektors, Ztschr. f. d. ges. exper. Med. 104: 705, 1939.
11. Mann, Hubert: A Method of Analyzing the Electrocardiogram, Arch. Int. Med. 25: 283, 1920.
12. Wilson, Frank N., Macleod, A. Garrard, and Barker, Paul S.: The T Deflection of the Electrocardiogram, Tr. A. Am. Physicians 46: 29, 1931.
13. Wilson, Frank N., Macleod, A. Garrard, Barker, Paul S., and Johnston, Franklin D.: The Determination and the Significance of the Areas of the Ventricular Deflections of the Electrocardiogram, AM. HEART J. 10: 46, 1934.

DIFFERENCES IN BLOOD PRESSURE VALUES DETERMINED BY INFLATING AND DEFLATING THE CUFF OF THE SPHYGMOMANOMETER

CAPTAIN ROBERT S. CUNNINGHAM, M.C.
ARMY OF THE UNITED STATES

IF ONE listens carefully for arterial tones, a different set of blood pressure readings will be found while the sphygmomanometer cuff is being inflated than will be found when the cuff is being deflated. Both maneuvers were employed in 200 out of 3,000 recent examinations, and the findings were recorded. The majority of the patients examined were white men of average height and weight between the ages of 20 and 50 years. They were chiefly ex-military personnel who were referred for routine examinations.

The procedure consisted of a period of thirty to sixty minutes' rest during which the history was taken. The patient was stripped for measurement of the height and weight and for inspection for scars and defects. He remained seated for examination of the eyes, ears, nose, and throat. He moved eight feet to another stool for determination of the temperature, the pulse rate, respiratory rate, and the blood pressure, and for examination of the heart and lungs. Thus, a sufficient period of rest following light activity was routine.

In making measurements of the blood pressure care was observed in placing the sphygmomanometer cuff on the left arm smoothly and in such a way that pressure would not force the lower edge of the cuff against the stethoscope, so that noise would not be produced. The cuff was inflated slowly until the first sound (diastolic reading) was audible. It was then inflated more rapidly, but smoothly, until the sounds disappeared (systolic reading). After raising the mercury column 30 to 40 mm. higher, the pressure was then determined in the usual manner with the mercury falling. Thus, the first sound to appear when the cuff was inflated corresponded to the last sound when it was deflated, and the last sound during inflation corresponded to the first sound on deflation.

In the second phase of inflation the mercury column was raised at a rate of 4 to 6 mm. per heartbeat. This permitted an error of 5 mm. in the readings. This may be considered as an objection to the test, but this error, as shown in Table I, is no more than a +6 mm. in the difference column and does not explain the minus differences that are found in those cases showing a lower systolic pressure by the standard method; nor does it explain the plus differences of 20 mm. or more. This error is unavoidable as some possible reflex mechanism is given time to exert its balancing influence if the rate of inflation is too slow. Thus, a bradycardia extends the error to the point of nullifying the test. No such error, however, occurs in the diastolic readings. While experimenting with

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TABLE I.

TYPE	CASE	PATIENT	DIAGNOSIS	A	B	DIFFERENCE
1	3	FLS	Hypertension	160	206	+46
				118	110	−8
2	18	JS	Arteriosclerosis	118	128	+10
				74	82	+8
3	8	JBB	Hypertension	210	220	+10
				130	130	0
4	176	HA	Trauma	120	120	0
				80	82	+2
5	44	FJS	Valvular heart disease	110	110	0
				86	84	−2
6	37	GHH	Pericarditis	118	118	0
				74	74	0
7	106	SM	Muscular atrophy	154	150	−4
				92	92	0
8	41	NON	Valvular heart disease	106	94	−12
				76	64	−12
9	79	FHW	Neurasthenia	100	94	−6
				66	70	+4

A = Readings taken during inflation of the sphygmomanometer cuff.
B = Readings taken during deflation of the sphygmomanometer cuff.

this test in some cases of hypertension it was observed that the systolic peak seemed to follow the cuff pressure. That is, the sounds might disappear at a certain level during inflation of the cuff, only to return if the inflation were stopped at that level; the sounds might disappear on further inflation and reappear at a higher level until a maximum point was reached beyond which there was no further rise.

In the standard method the disappearance of sound was recorded as the diastolic reading. An interesting observation was the fact that, in most cases, the cuff pressure could be left for thirty seconds or more immediately below the first diastolic reading and no sound could be heard even though the diastolic level by the standard method was below the first reading. For example, as the mercury was rising the first sound came in at 82 mm. and as it was falling the last sound was heard at 78 mm., but a repetition of the procedure and maintenance of the cuff pressure at 80 mm. for about ten seconds did not elicit a sound. It was noted that when there was a difference between the change of sound and the disappearance of sound during deflation, the diastolic reading during inflation more nearly corresponded to the change of sound. From this it is believed that the change of sound marks the true diastolic pressure and the sound produced with less cuff pressure is caused by vascular dilatation. This may be a compensation for an increased systolic pressure caused by a reflex stimulation arising from the pressure on the arteries in the arm during the sphygmomanometry. That such a reaction occurs is denied by Hamilton and his co-workers[1] who measured the intra-arterial pressure with a needle in the artery and compared it with sphygmomanometer measurements taken simultaneously in the other arm. He reported that the two methods gave reasonably identical results. It is possible, however, that a needle in an artery establishes the same sort of sensory stimulus as pressure on the artery by a sphygmoma-

nometer cuff. Kotte and his associates[2] wrote, "The only pain which the subjects noted was felt as a brief twinge at the moment of arterial puncture." At least the intra-arterial method is not stimulus-free and it is possible that every known method of measuring blood pressure affects the tension by its mere application.

In this series of approximately 3,000 patients only 200 were suitable for study for the same reasons given by numerous investigators[3-8] as sources of error in sphygmomanometry, namely: excessive obesity or emaciation, weak Korotkow sounds, high noise level of the room, noisy inflating mechanism, and involuntary tremors of the subject. Some subjects were rejected because the procedure of examination deviated from the routine, time was at a premium, or the pulse was too slow.

In this series nine types of response to the pressure of the sphygmomanometer cuff were noted consisting of no change, a rise, or a fall in the systolic and/or diastolic pressures. An example of each type is shown in Table I. Of the first type (in which the systolic pressure was higher and the diastolic lower by the deflation than by the inflation method) there were 109 cases (54.5 per cent); of the second type, 53 (26.5 per cent); the third, 12 (6 per cent); the fourth, one (0.5 per cent); the fifth, two (1 per cent); the sixth, three (1.5 per cent); the seventh, one (0.5 per cent); the eighth, 15 (7.5 per cent); and the ninth, four (2 per cent). In the first group the greatest differences were noted, chiefly from cases of hypertension. All of the hypertensive conditions fell in Groups 1, 2, or 3.

SUMMARY AND CONCLUSIONS

A method of measuring the blood pressure for comparison with the standard procedure is described. Compression by the sphygmomanometer cuff appears to produce a change in the blood pressure so that the systolic reading usually is higher and the diastolic lower after the cuff is inflated. It is suggested that this apparent response is the result of a stimulus from the vascular autonomic system reflexly affecting the cardiac and vascular tone and that the type and degree of response depends upon which fibers are hyperirritable at the time.

REFERENCES

1. Hamilton, W. F., Woodbury, R. A., and Harper, H. T.: Physiologic Relationship Between Intrathoracic, Intraspinal, and Arterial Pressures, J. A. M. A. 107: 853, 856, 1936.
2. Kotte, J. Harold, Iglauer, Arnold, and McGuire, Johnson: Measurements of Arterial Blood Pressure in the Arm and Leg, AM. HEART J. 28: 476, 1944.
3. American Heart Association: Standardization of Blood Pressure Readings, AM. HEART J. 18: 95, 1939.
4. Hines, E. A., Jr., and Brown, G. E.: The Cold Pressor Test for Measuring the Reactibility of the Blood Pressure, AM. HEART J. 11: 1, 1936.
5. Allegretti, Anthony J.: Blood Pressure as Affected by Altitude, M. Bull. Vet. Admin. 19: 290, 1943.
6. Rappaport, Maurice B., and Luisada, Aldo A.: Indirect Sphygmomanometry, J. Lab. & Clin. Med. 29: 638, 1944.
7. Ragan, Charles and Bardley, James III: The Accuracy of Clinical Measurements of Arterial Blood Pressure, Bull. Johns Hopkins Hosp. 69: 504, 1941.
8. Gambill, Earl E., and Hines, Edgar A., Jr.: Blood Pressure in Arm and Thigh of Man, AM. HEART J. 28: 763, 1944.

Clinical Reports

METASTATIC CARCINOMA AS A CAUSE OF CONSTRICTIVE PERICARDITIS

Report of a Case

Major Joseph J. Wallace, M.C., and Major Robert Bruce Logue, M.C.
Army of the United States

REPORTS of metastatic tumors of the pericardium producing chronic cardiac compression with secondary right-sided heart failure are quite rare. The following case of primary bronchogenic carcinoma with metastasis to the pericardium is an example of such a case.

CASE REPORT

A Negro man, 41 years of age, was admitted to an Army general hospital on Aug. 24, 1943. The past personal and family history were not significant. In May, 1943, the patient gradually developed shortness of breath on exertion, moderate pain in the substernal region and near the right shoulder blade, occasional productive cough with expectoration of clear mucoid sputum, night sweats, and anorexia, and lost 30 pounds in weight. Because of the persistence of these symptoms, the patient reported to the dispensary and was admitted to the station hospital. Examination at that time revealed enlarged lymph glands in the cervical and supraclavicular regions, impaired resonance over the right upper anterior chest and mediastinum and moist râles throughout the chest. There was x-ray evidence of enlargement of the superior mediastinum and biopsy of a cervical lymph node was reported to show hyperplastic lymphadenitis. He was transferred to an Army general hospital.

Examination at the time of admission revealed a chronically ill, emaciated patient with evidence of enlargement of the superior mediastinum and moderate clubbing of the fingers and toes. During the first part of his hospital stay, his course was essentially uneventful, except for a troublesome "brassy" cough and an occasional slight hemoptysis. A biopsy of a right axillary node was reported as reactive lymphadenitis, but, upon review by another source, was thought to represent an early stage of Boeck's sarcoid.

Repeated urinalyses were essentially normal, and several blood counts revealed a mild secondary anemia with a leucocyte count ranging from 6,000 to 11,000, with a normal differential. The sedimentation rate was persistently elevated to 60 mm. in one hour. Seven sputum examinations were negative for tubercle bacilli. The Kahn reaction on the blood and spinal fluid was negative. The total protein of the blood serum was 5.9 Gm. per 100 c.c., with an albumin-globulin ratio of 1:1.3. Values for serum calcium, phosphorus, and phosphatase were normal. A biopsy of the bone marrow revealed atrophic marrow.

An x-ray of the chest in August, 1943, revealed a tumor mass involving the superior mediastinum with enlargement of adjacent lymph nodes. The cardiac silhouette was nor-

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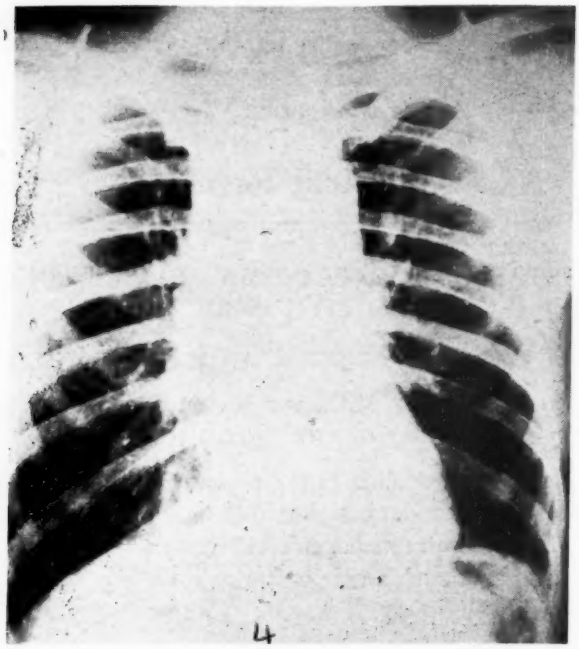

Fig. 1.—Film taken July 11, 1943, showing enlargement of the superior mediastinum and right hilar region.

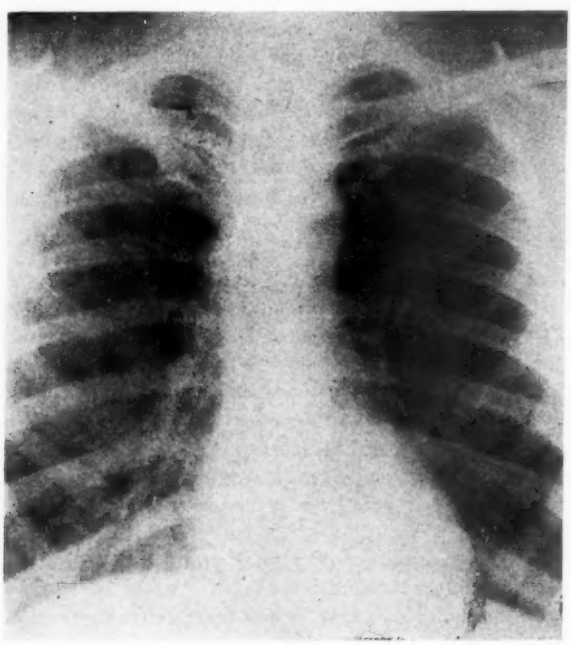

Fig. 2.—Film taken on induction shows enlarged glands in the right hilum and right para-aortic area.

mal in size and shape. X-ray examination of the long bones and hands revealed hypertrophic pulmonary osteoarthropathy.

About five months after onset, in October, 1943, the patient developed a sharp precordial pain aggravated by movement and inspiration. A loud, to-and-fro, leathery friction rub was heard over the precordium. Serial electrocardiograms showed evidence of acute pericarditis, and, in addition, persistent low amplitude of the QRS complexes in all leads, suggesting tamponade or chronic pericarditis. The area of cardiac dullness increased markedly to the right and left. The apex impulse was palpated diffusely in the fifth intercostal space. The heart sounds were well heard and the first sound at the mitral area was accentuated.

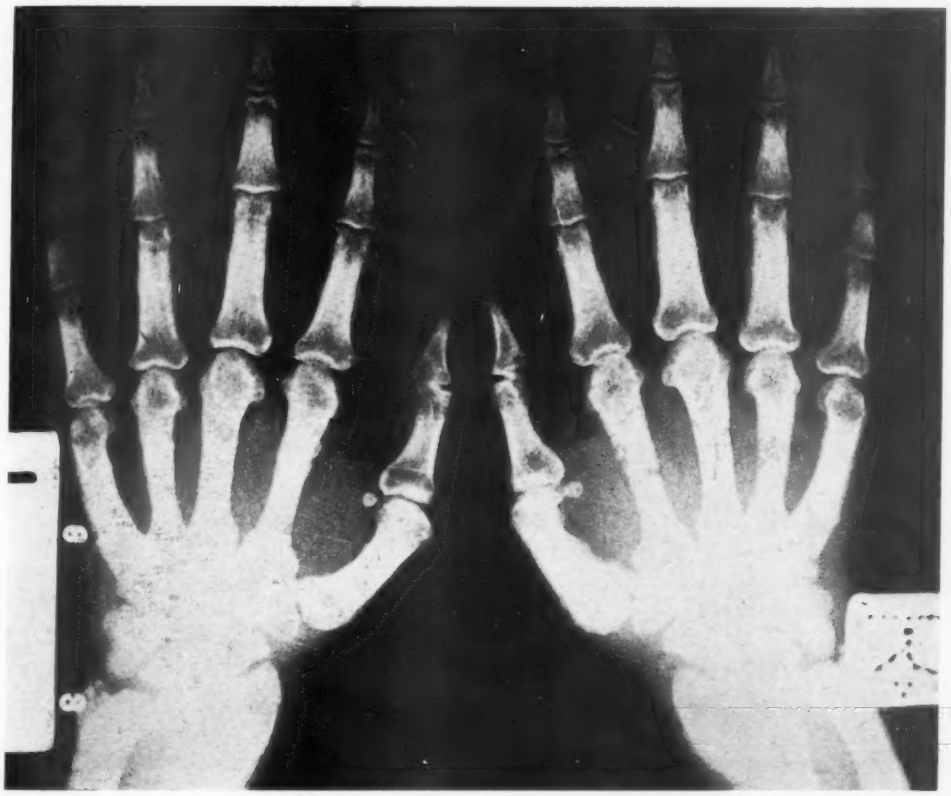

Fig. 3.—Films of hands showing hypertrophic pulmonary osteoarthropathy involving the shafts of the metacarpal bones.

The pulmonic second sound was not remarkable. The blood pressure measured 116/70. The neck veins were strutted in the recumbent position but were not distended in the upright position. The venous pressure was 150 mm. of saline. Fluoroscopy revealed marked enlargement of the cardiac silhouette, both to the right and to the left, diminished pulsations in the region of the left ventricle, and an irregularity along the left cardiac border suggesting a nodule in the pericardium. About one month after the onset of the pericarditis, there gradually developed a marked pitting edema of both legs, extending as high as the knees. The liver was palpable 3 fingerbreadths beneath the costal margin. The patient, during this period, had occasional episodes of dyspnea for which oxygen was given with relief, but during the greater portion of the time, he was able to lie flat in bed without difficulty. At one time, a small pleural effusion developed on the right side. It was

believed that the clinical features were those of right-sided heart failure. These symptoms gradually subsided and the further course was uneventful until Jan. 15, 1944, when he experienced increasing dyspnea. By physical examination and by x-ray films, taken in both inspiration and expiration, it was determined that he had an acute emphysema involving the entire right lung, due to a ball valve mechanism in the right main stem bronchus. His condition grew steadily more serious, and he expired on Feb. 23, 1944.

Necropsy examination revealed an extensive bronchogenic carcinoma, primary in the right main stem bronchus, with obstructive emphysema of the right lung. The pericardium presented an extraordinary appearance. The visceral and parietal pericardium was edematous and adherent. There was extensive infiltration of the pericardium by firm, nodular,

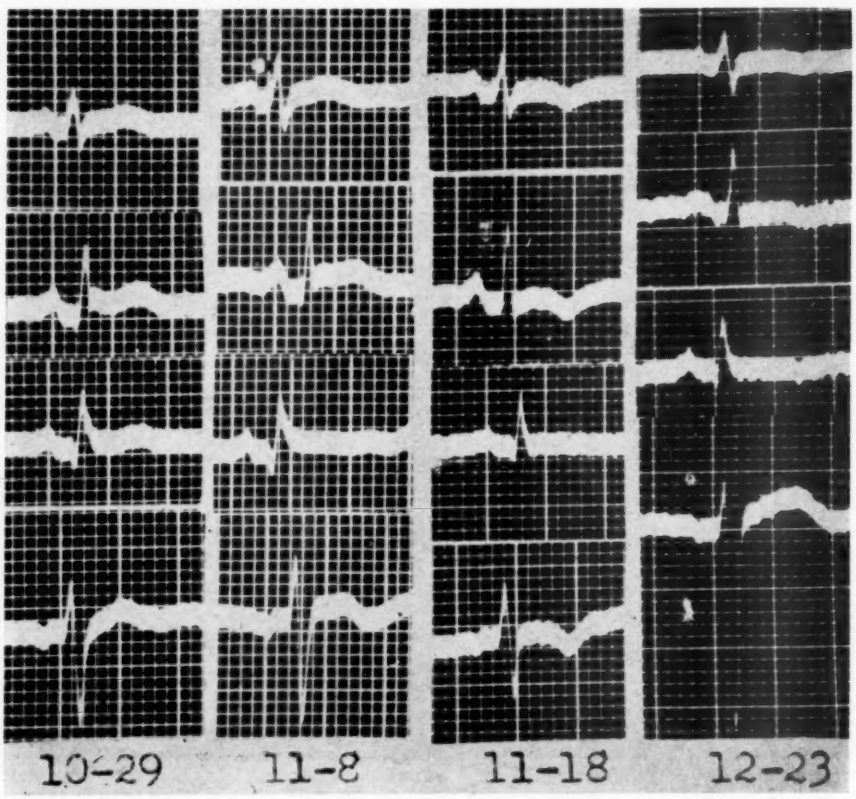

Fig. 4.—Note the serial electrocardiographic changes of acute pericarditis with the addition of low amplitude of all QRS complexes in the standard leads, and persistent inversion of the T waves suggesting chronic pericarditis.

gray, tumor tissue. This formed a mass, averaging 2.5 cm. in thickness, that completely encased the heart. The heart appeared to be normal in size and there was no hypertrophy of either ventricle. The myocardium was not invaded by tumor tissue. Microscopic examination revealed the primary and metastatic tumors to be composed of solid masses of polygonal cells with vesicular nuclei with moderate anaplasia and irregular mitoses. There was a suggestion of an acinar arrangement in some areas. The pathologic diagnosis was: (1) bronchogenic carcinoma, Grade 2, of the right main bronchus; (2) metastases to mediastinal lymph nodes, pericardium, and adrenal glands; (3) emphysema of the right lung; and (4) hypertrophic pulmonary osteoarthropathy.

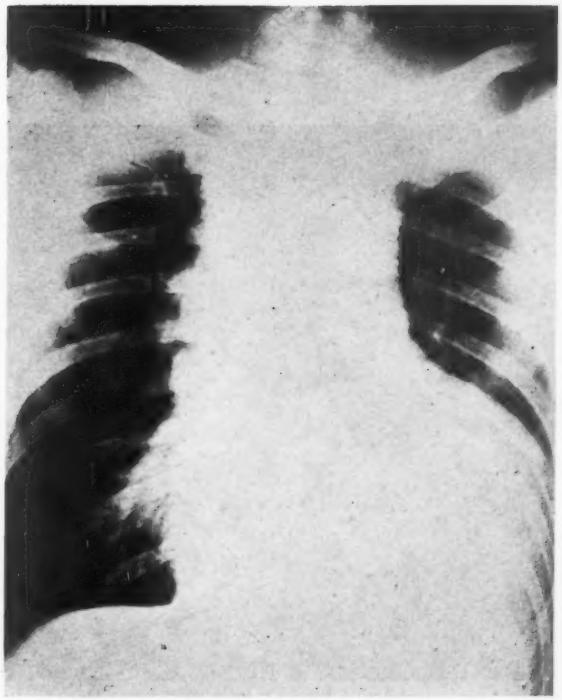

Fig. 5.—Film taken Nov. 2, 1944, showing marked enlargement of cardiac silhouette to the left and enlargement of the superior mediastinum. Note enlarged glands in right hilar region.

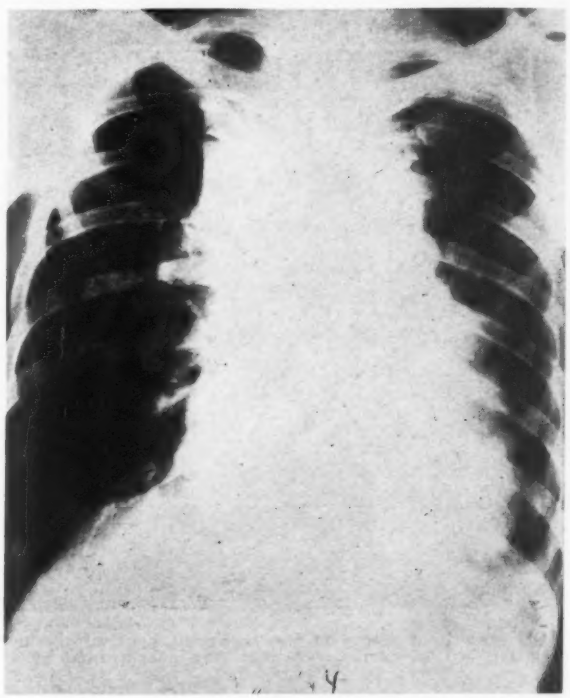

Fig. 6.—Film taken Jan. 21, 1944, showing emphysema of right lung with widening of intercostal spaces and shifting of mediastinum to the left. Note the irregular cardiac shadow and superior mediastinal mass.

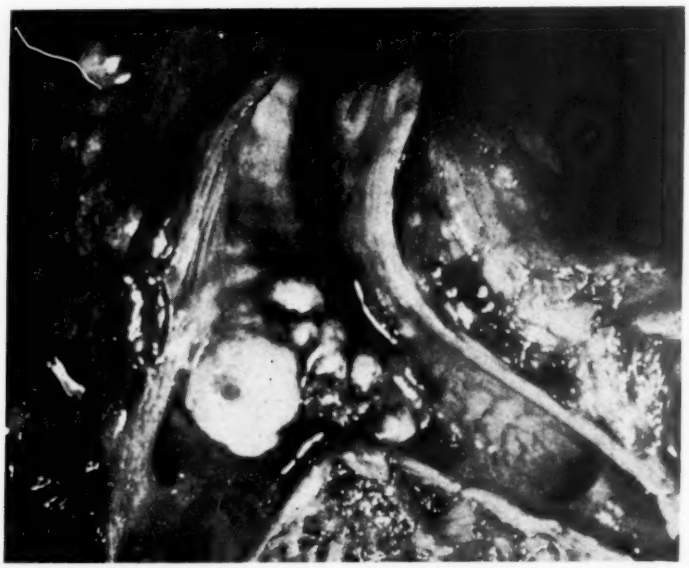

Fig. 7.—Note primary site of bronchogenic carcinoma in right main stem bronchus.

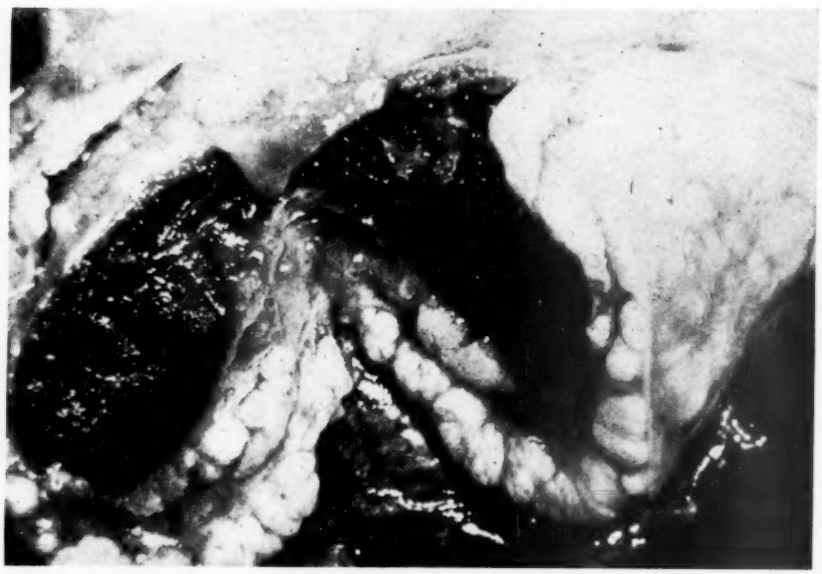

Fig. 8.—Note the dense growth of tumor in the pericardium about the heart which has been opened. The heart was of normal size and was not invaded by tumor tissue.

COMMENT

In view of the history and findings at the time of admission, bronchogenic carcinoma was thought to be present. Later, the diagnosis of sarcoid, as a result of a biopsy of an axillary gland, led to some confusion and it was thought that the clinical picture could be explained on this basis. The occurrence of acute pericarditis during the course of the illness was compatible with either disease entity. At the time of the occurrence of congestive heart failure, the clinical picture was that of right-sided heart failure. This was thought to be due to cardiac compression or to chronic cor pulmonale, secondary to pulmonary infiltration or extrinsic pressure on the pulmonary artery. Following fluoroscopy, it was thought that the most likely explanation was chronic compression of the heart by tumor tissue. The electrocardiographic changes were of interest, demonstrating the S-T segment changes of acute pericarditis as well as low amplitude of all QRS complexes, such as is seen in chronic pericarditis or in the presence of an effusion. The T waves subsequently became inverted in all leads, and these changes persisted. At no time was an arrythmia, such as auricular fibrillation, noted. This was noted in 38 per cent of Harrison and White's series.[1]

Reports of metastatic tumors of the pericardium are not uncommon; however, obliteration of the pericardial cavity by such a process is rare. The production of the syndrome of constrictive pericarditis is even more rare. Scott and Garvin[2] reported involvement of the pericardium by metastases in 61 of 1,082 cases of malignancy in 11,100 consecutive autopsies. The heart was involved in 79 instances, the heart and parietal pericardium together in 22, and the heart or parietal pericardium, or both, in 118. The bronchus and breast were the most common sites of primary tumor. In only one instance was the pericardial cavity obliterated. Seven cases showed myocardial insufficiency and none were reported to be due to cardiac compression. Yater[3] reported 11 cases of neoplasm involving the pericardium and in no case was the pericardial cavity obliterated. Henninger[4] reported four cases of metastasis to the pericardium, but none exhibited congestive cardiac failure. The parietal pericardium in Case 2 of his series was closely adherent to the epicardium. Langford and Thomas[5] reported a case in which the pericardial cavity was obliterated by metastases from a hypernephroma, but cardiac failure was not present. Leaman[6] reported a case of bronchogenic carcinoma with metastases to the heart, with obliteration of the pericardium, which completely encased the heart and produced cardiac failure. Beck[7] reported two cases of chronic cardiac compression from invasion of the parietal pericardium and mediastinum by sarcoma. The pericardium was thickened, but not adherent to the heart. Thus, it is seen that neoplastic involvement of the pericardium may be a rare cause of constrictive pericarditis.

SUMMARY

The syndrome of constrictive pericarditis may be produced by neoplastic involvement of the pericardium. Such a process should be suspected when the

symptoms of predominant right-sided heart failure appear during the course of a malignancy, in the absence of other usual causes of such failure. A case of bronchogenic carcinoma with metastasis to the pericardium demonstrating this condition is reported.

REFERENCES

1. Harrison, M. B., and White, P. D.: Chronic Constrictive Pericarditis: A Follow-Up Study of Thirty-Seven Cases of Pericarditis, Ann. Int. Med. **17**: 790, 1942.
2. Scott, Roy W., and Garvin, Curtis F.: Tumors of the Heart and Pericardium, AM. HEART J. **17**: 431, 1939.
3. Yater, Wallace M.: Tumors of the Heart and Pericardium; Pathology, Symptomatology and Report of Nine Cases, Arch. Int. Med. **48**: 627, 1931.
4. Henninger, Ben R.: Clinical Aspects of Pericardial Metastasis, Ann. Int. Med. **7**: 1359, 1934.
5. Langford, John A., and Thomas, E. Perry: Obliterated Pericardium by Hypernephroma Metastasis, South. M. J. **26**: 929, 1933.
6. Leaman, Wm. G.: Management of the Cardiac Patient, Philadelphia, 1940, J. B. Lippincott Co., p. 432.
7. Beck, Claude S.: Acute and Chronic Compression of the Heart, AM. HEART J. **14**: 515, 1937.

THE CURE OF SUBACUTE BACTERIAL ENDARTERITIS BY SURGICAL LIGATION IN A PATIENT WITH PATENT DUCTUS ARTERIOSUS COMPLICATED BY THE PRESENCE OF MULTIPLE CONGENITAL CARDIAC DEFECTS

Report of a Case

Robert F. Ziegler, M.D.
Detroit, Mich.

IT IS generally agreed that the absence of typical murmurs constitutes a contraindication to surgical intervention in cases of suspected patent ductus arteriosus. However, since typical murmurs are absent in nearly a third of the cases, and the incidence of subacute bacterial endarteritis ranges as high as 50 per cent in reported series, there must consequently be a considerable number of cases in which the decision for or against surgical treatment is difficult. A decision in favor of surgery may be made in such cases under two conditions. The first of these is that the infectious agent is resistant to sulfonamide or penicillin therapy. The second is that no other congenital defect is present which requires the open ductus as a compensatory mechanism.

It would seem reasonable to assume that the presence of multiple congenital defects would be a rather frequent cause for the occurrence of unusual physical signs, or the absence of typical findings, in cases of patent ductus arteriosus. In such instances excellent judgment is required in selecting a patient suitable for surgical treatment. A case is herewith reported in which an infected patent ductus occurred with atypical murmurs, in association with multiple congenital cardiac defects, in which the infectious agent was resistant to penicillin, and in which cure was accomplished by surgical ligation of the patent ductus arteriosus.

CASE REPORT

The patient, a 17-year-old white girl, was admitted to Henry Ford Hospital on April 14, 1944, with a chief complaint of persistent fever and "heart trouble." The present illness began approximately four months previously, at which time the patient experienced an influenza-like illness, the duration of which was three weeks. This was followed by recurrent bouts of fever, on occasion as high as 102° F. She had had fleeting abdominal pain, but no chest pain, night sweats, weight loss, or evidence of embolic phenomena in either systemic or pulmonary circulation. The past history was negative except for the presence of a heart murmur, known of since the age of six months, and episodes of paroxysmal tachycardia. The growth had been normal; exercise tolerance was average; and there was no history of rheumatic fever.

From the Cardio Respiratory Division, Henry Ford Hospital, Detroit, Mich.
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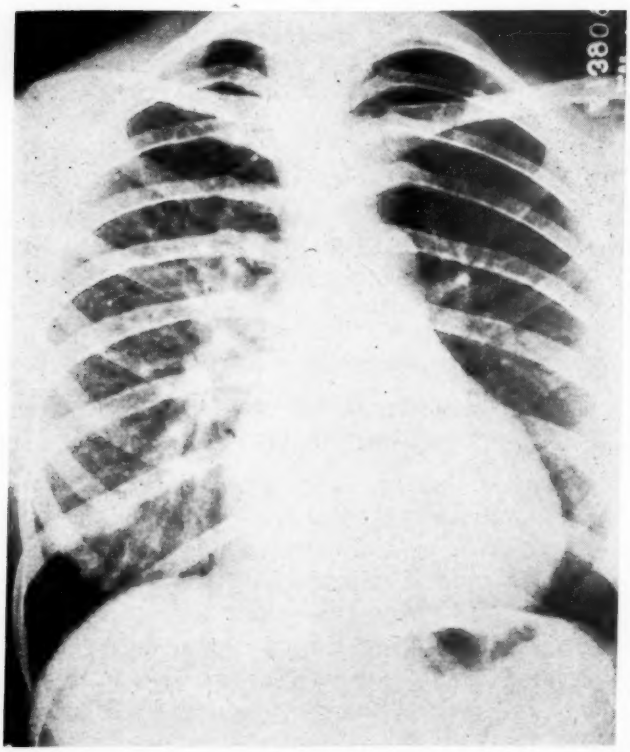

Fig. 1.—X-ray of the chest before surgical ligation (May 23, 1944).

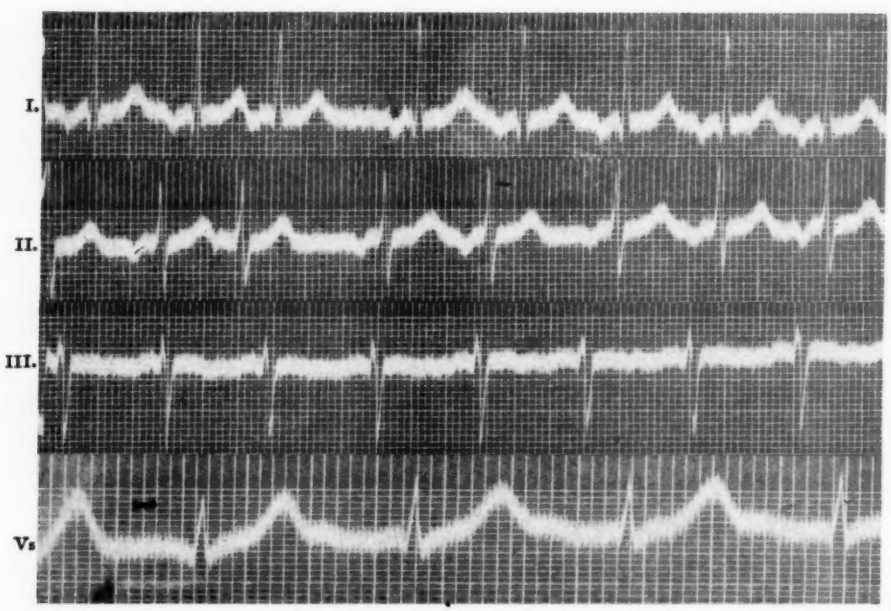

Fig. 2.—Electrocardiogram, taken May 23, 1944, showing inverted P waves in standard Leads I and II.

On physical examination the patient appeared to be a well-developed, well-nourished white girl of the stated age, who did not appear acutely ill. The head and neck were entirely normal. The mucous membranes were of good color. No petechiae were visible. There was no abnormal lymphadenopathy. On examination of the chest, the lung fields were resonant to percussion, the breath sounds were normal throughout, and no râles were heard. The heart was slightly enlarged to the left, the left border of cardiac dullness measuring 11 cm. from the midsternal line in the fifth intercostal space. There was no widening of the upper mediastinum. A systolic thrill was palpable over the base of the heart. On auscultation there was a loud, rough systolic murmur heard over the entire precordium, loudest at the second and third intercostal spaces at the left sternal border. This murmur was transmitted widely, and could be heard over the entire chest both anteriorly and posteriorly. The pulmonic second sound was accentuated, and there was a short diastolic blowing murmur heard at the third intercostal space at the left sternal border. The cardiac rhythm was regular. The blood pressure at rest was 120/60; immediately after exercise it was 120/40 to 10. Examination of the abdomen was essentially negative. The liver and spleen were not palpable. No abdominal masses or tenderness were noted. The extremities were normal. Pelvic examination was not done.

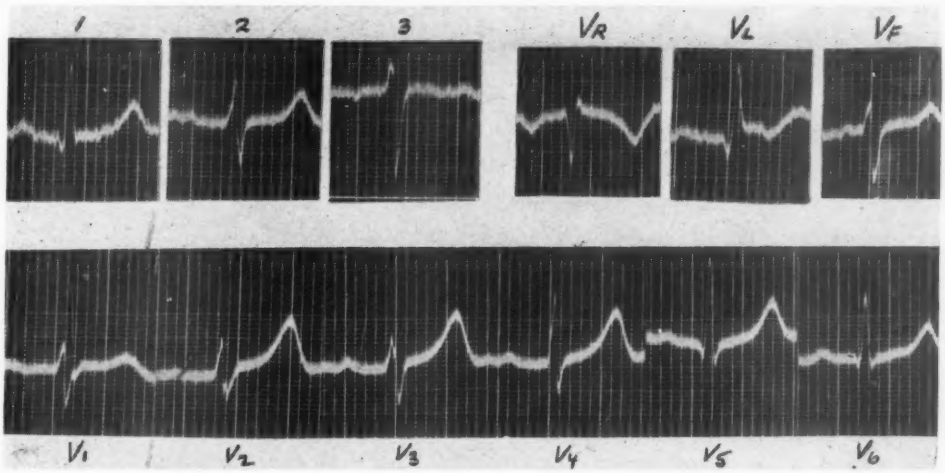

Fig. 3.—Electrocardiogram taken May 24, 1944. Standard extremity leads. Unipolar extremity Leads V_R, V_L, and V_F. Precordial Leads V_{1-6}.

The initial laboratory examinations included the following: Kline exclusion test, negative; hemoglobin, 13.1 Gm. per cent; erythrocytes, 4,370,000; leucocytes, 9,100 per cubic millimeter, with 65 per cent polymorphonuclear leucocytes and 35 per cent small lymphocytes; blood sedimentation rate, 38 mm. per hour; hematocrit, 43 per cent; urine specific gravity, 1.028, alkaline reaction, negative for albumin, sugar, casts, and red blood cells; blood nonprotein nitrogen, 28.1 mg. per cent; blood sugar, 78 mg. per cent; routine stool examination, negative. Two successive blood cultures were positive for hemolytic *Staphylococcus albus.*

Fluoroscopy of the chest revealed slight cardiac enlargement involving both ventricles, chiefly the left. There was increased amplitude of pulsation of the left ventricle, aorta, and pulmonary conus. The latter was not unusually prominent. There was partial obliteration of the aortic window. The transverse diameter of the heart measured 11.5 cm., and the internal transverse diameter of the chest measured 21.9 centimeters. The predicted transverse diameter of the heart (Hodges and Eyster) was 10.49 centimeters. The electrocardiogram showed left axis deviation ($R_1 + S_3 = 2.8$ mv.), with normal ventricular

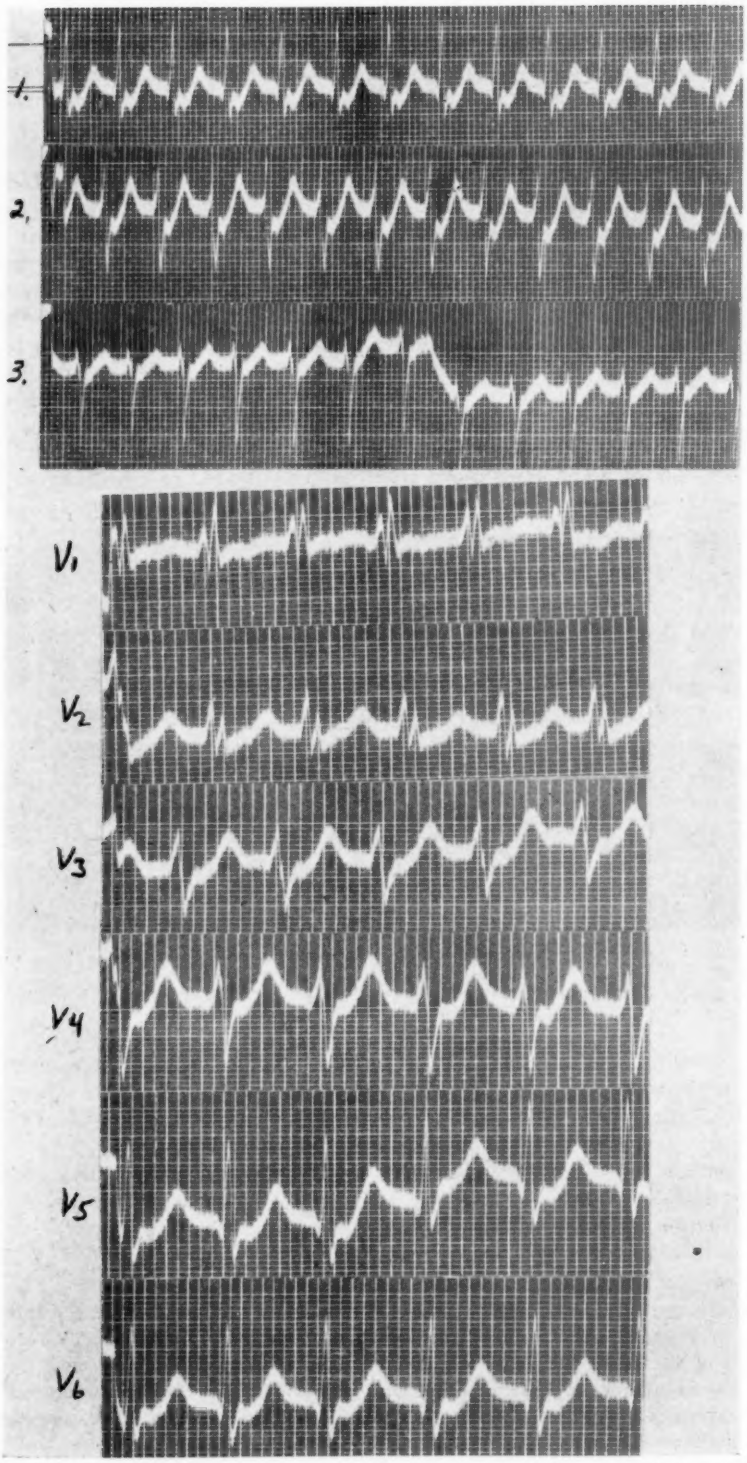

Fig. 4.—Electrocardiogram, taken Jan. 28, 1945, during paroxysm of auricular tachycardia.

complexes. P-R interval and QRS interval were normal. The form of the P waves varied considerably, on one occasion being inverted in standard Leads I and II (Fig. 2), on another occasion being normally upright (Fig. 3), and finally disappearing during a paroxysm of auricular tachycardia (Fig. 4). Phonocardiography proved the presence of the short diastolic murmur (Fig. 5). The initial venous pressure measured 9 cm. (saline) with no rise on right upper quadrant compression. The arm-to-tongue circulation time (decholin) measured 13 seconds; the arm-to-lung circulation time (ether) measured 8 seconds.

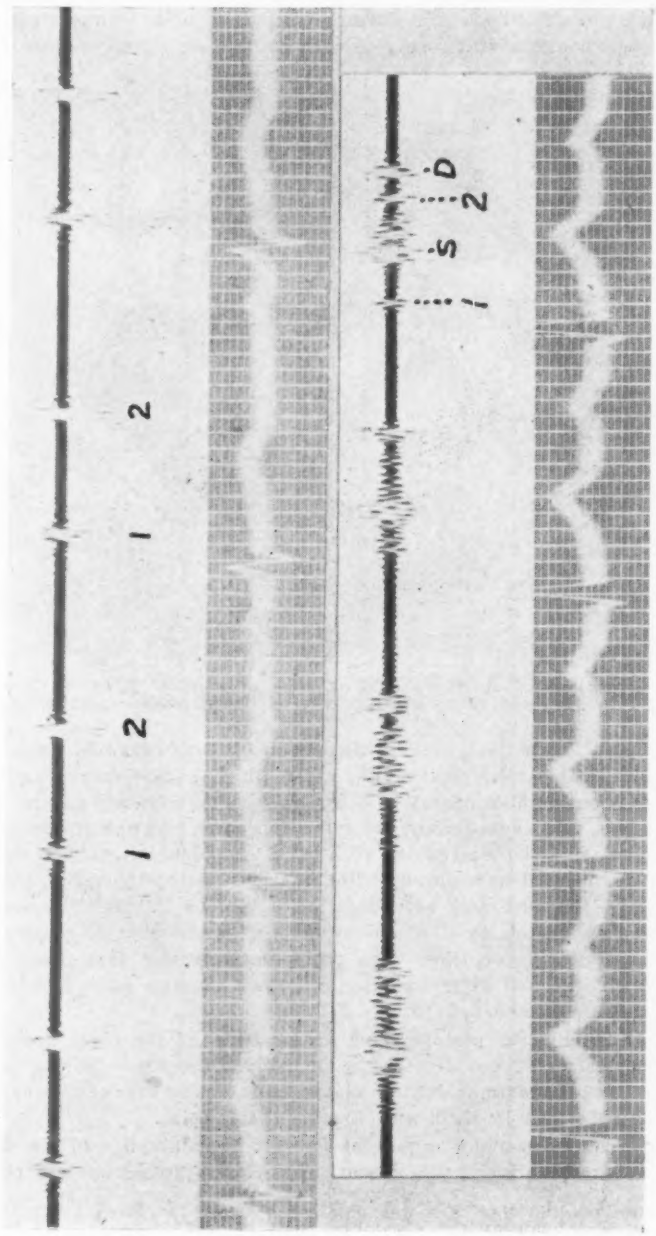

Fig. 5.—Simultaneous phonocardiogram and electrocardiogram taken preoperatively (lower record). Normal control above. *1*, First heart sound; *2*, second heart sound; *S*, systolic murmur; and *D*, diastolic murmur.

On the basis of the above findings the diagnosis of subacute bacterial endarteritis with patent ductus arteriosus was made. The presence of a concomitant congenital cardiac defect was considered likely.

Although the patient did not appear toxic or acutely ill, her temperature ranged daily between normal and 103.8° F. until the institution of penicillin therapy. The latter was begun on the twelfth hospital day and continued for twelve days prior to surgery. During the first twenty-four hours 200,000 units were given by continuous intravenous drip, subsequent dosage being 12,500 units intramuscularly every three hours, day and night.* Although the patient remained afebrile during this period, blood cultures after ten days of penicillin administration were still positive for hemolytic *Staphylococcus albus.*

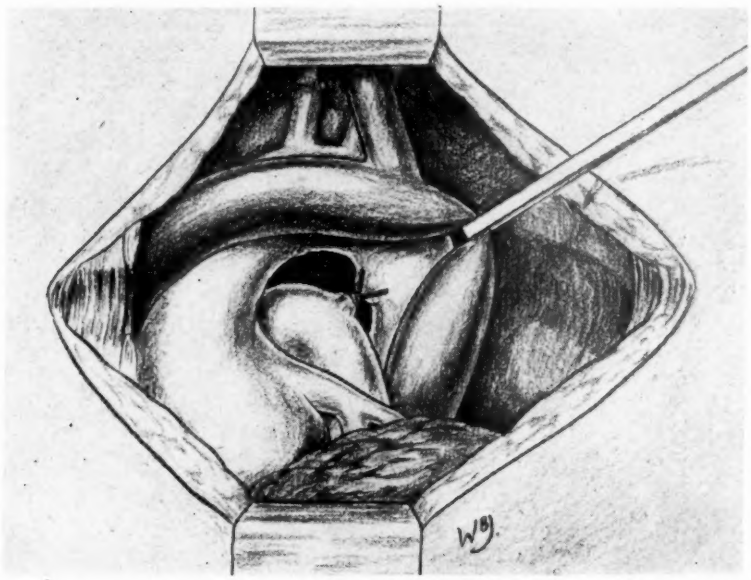

Fig. 6.—Artist's conception of operative field at time of surgical ligation. Anomalous left vena cava has been retracted from site of ligated ductus arteriosus.

On May 8, 1944, the patient was operated upon by Dr. Conrad R. Lam. The patent ductus was doubly ligated with heavy silk, after which a cellophane band was placed snugly around it. Considerable operative difficulty was encountered due to the presence of a large anomalous vein immediately overlying the aorta and the region of the ductus (Fig. 6). This appeared to be a left-sided vena cava. A palpable thrill, previously present over the ductus, disappeared immediately after ligation. Before operation the blood pressure measured 140/40; immediately after ligation it became 120/70. The surgical procedure was tolerated very well by the patient, and an uncomplicated recovery followed. Penicillin was administered for three days postoperatively and then discontinued. The patient remained afebrile and asymptomatic, and blood cultures have remained negative, the last one being taken on Feb. 5, 1945.

The physical findings on postoperative examination of the chest are of particular interest. The heart size did not decrease appreciably. There was still a very loud and widely distributed systolic murmur, but the maximum intensity over the lower right sternal border was louder and a systolic thrill was palpable at this point.

The pulmonic second sound was present but not accentuated, and the diastolic murmur, demonstrated preoperatively, was absent. The electrocardiogram was not essentially

*The penicillin used in this case was obtained through Dr. Roy D. McClure from Dr. Chester S. Keefer, Chairman of the Committee on Chemo-Therapeutic and Other Agents, Division of Medical Sciences, National Research Council.

different from that recorded prior to surgery. On fluoroscopic examination the cardiac silhouette had not changed appreciably, though the amplitude of pulsation seemed less marked. The venous pressure and circulation time determinations remained normal. A diagnosis was made of a patent interventricular septal defect.

The patient has remained well with the exception of occasional episodes of auricular paroxysmal tachycardia, now much less frequent than before surgery; and a ruptured ovarian cyst which required surgical excision Jan. 28, 1945. Her present physical condition is excellent; she has a perfectly normal exercise tolerance.

SUMMARY

A case of subacute bacterial endarteritis with patent ductus arteriosus, patent interventricular septal defect, and anomalous left vena cava, in which cure was effected by surgical ligation of the patent ductus, is reported.

Surgical treatment, when otherwise contraindicated by atypical physical signs, should be considered when the infecting organism is resistant to chemotherapy and when a complicating congenital defect, requiring a patent ductus as a compensatory mechanism, is not present.

MUMPS MYOCARDITIS

Review of Literature and Report of Case

George E. Felknor, M.D., and Roscoe L. Pullen, M.D.
New Orleans, La.

A RECENT paper by Wendkos and Noll[1] brought attention to the existence of acute myocarditis ascribable to mumps which could be recognized electrocardiographically during the convalescent period. In the case reported by them, however, no clinical signs of myocardial disease could be demonstrated. The purpose of this communication is to report a case, apparently of mumps myocarditis, which manifested both clinical and electrocardiographic evidences of myocardial involvement.

Scant attention has been given to the possibility of myocardial involvement during an acute episode of mumps. Pujol,[2] a French military surgeon, first suggested in 1918 that the virus of mumps might conceivably affect the myocardium. During a period of nine months he observed a total of 450 cases of mumps and in twelve of these he discovered some disturbances in the circulatory system. However, nine of these patients were eliminated from his consideration in view of other etiological factors for their heart disease. The remaining three patients complained of substernal pain and dyspnea during the convalescent period and, since no other explanation could be found, Pujol suspected myocardial involvement from mumps. Unfortunately, he did not have electrocardiograms to corroborate his suspicions. In 1932 Manca[3] concluded from post-mortem observations that mumps may produce an acute interstitial myocarditis which could be distinguished from other forms by the fibrinous reaction which he believed to be peculiar to this disease.

Stimulated by these observations, Wendkos and Noll[1] undertook a random cardiac survey of fifteen soldiers convalescing from mumps. They demonstrated electrocardiographic changes in one patient (6.7 per cent) as manifested by sinus bradycardia, T-wave changes, and prolongation of the P-R interval. They further demonstrated temporary shortening of the A-V conduction time following the administration of atropine sulfate. This effect was interpreted as evidence that the prolonged P-R interval resulted from an increased vagal tone, a response similar to that observed in active rheumatic carditis.[4-6] Complete recovery of their patient occurred in seven weeks.

The following case report is presented to point out both clinical and electrocardiographic evidences of acute myocarditis following mumps.

From the Department of Medicine, Tulane University of Louisiana School of Medicine, and Charity Hospital of Louisiana at New Orleans.
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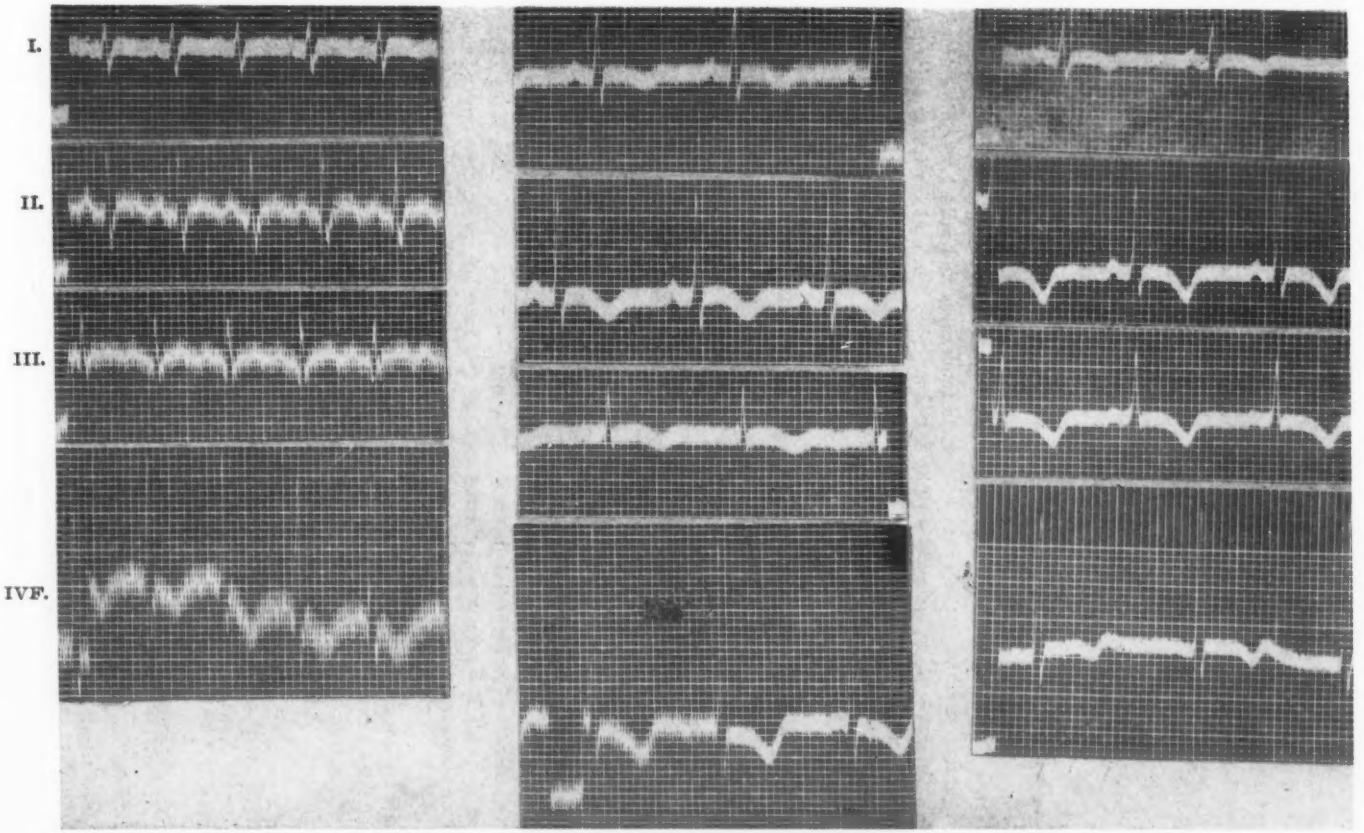

Fig. 1.—Electrocardiograms of a 14-year-old white boy with mumps and myocardial disease. *A*, Electrocardiogram made on March 27, 1944, eight days after the onset of parotid swelling. *B*, Electrocardiogram made on March 31, 1944, revealing acute myocarditis. *C*, Electrocardiogram made on April 25, 1944, revealing slight change from previous one. (See text for complete description.)

CASE REPORT

A. H., Jr., a 14-year-old white boy, entered Charity Hospital on March 26, 1944, complaining of fever, weakness, and swelling of both testicles. He stated that seven days previously his neck began to swell beneath the ears. The swelling attained considerable size. However, the patient did not go to bed and continued to be ambulatory. Three days later, the patient was forced to take to bed with high fever. The same day he developed soreness over the abdomen with intense pain on both sides of the abdomen extending from the border of the ribs downward to the inguinal regions. He felt nauseated and vomited several times. On the day of admission, both testicles began to swell.

Upon admission, physical examination revealed a well-developed, well-nourished white boy of the stated age who preferred to lie in bed on one side and maintained flexion of both legs. The temperature was 104° F., the pulse rate was 130, the respirations were 30 per minute, and the blood pressure was 100/70. The positive findings of the physical examination were as follows: slight swelling of the right parotid gland; muffled bronchovesicular breath sounds with a few râles in both bases posteriorly; a tachycardia (130 per minute) and a gallop rhythm at the apex; epigastric tenderness and mild lower abdominal tenderness; liver palpable 3 cm. below the right costal margin; bilateral testicular enlargement up to four times normal size; and a positive Babinski's reflex on the left side.

The laboratory data were as follows: leucocyte count of 12,930 per cubic millimeter with 90 per cent polymorphonuclears, 8 per cent lymphocytes, and 2 per cent monocytes; urinalysis, no abnormalities; carbon dioxide combining power of the blood, 30 volumes per cent; blood urea nitrogen, 19.6 mg. per 100 c.c.; fasting blood sugar, 129 mg. per 100 c.c.; negative blood Kline and Kolmer tests for syphilis; a negative blood culture; negative blood agglutination tests for *Eberthella typhi, paratyphi A* and *B, Brucella melitensis, Brucella abortus,* and *Bacillus proteus X 19.* A roentgenogram of the chest upon admission revealed an increase in the lung markings suggestive of an acute respiratory infection.

Because of the tachycardia and gallop rhythm at the apex, an electrocardiogram (Fig. 1, *A*) was taken and was interpreted by Dr. James L. Gouaux, cardiologist at Charity Hospital, as follows: auricular and ventricular rate 156 per minute; sinus tachycardia; slight slurring of the QRS complexes; slight shift upwards of the S-T segments in Leads I, II, and III; low T waves throughout with inversion of T_1 and T_4; and definite electrocardiographic evidence of myocardial disease. This was repeated seven days later (Fig. 1, *B*) at which time all T waves were inverted and the Q-T interval was at the upper limit of normal. This electrocardiogram was interpreted as compatible with subacute pericarditis and myocarditis.

The patient's course in the hospital was essentially uneventful. Because of somnolence, a spinal fluid examination was made which was within normal limits. The therapy was entirely supportive and symptomatic for mumps orchitis. The patient became afebrile on the third day and remained so until he was discharged on April 4, 1944.

He returned to the hospital on April 26, 1944, for a cardiac checkup. No pertinent physical findings were noted. The electrocardiogram (Fig. 1, *C*) was essentially the same as a previous one on April 4, 1944.

DISCUSSION

Evidence for the diagnosis of acute myocarditis in this patient is based upon the presence of a probable etiological factor, an acute onset, gallop rhythm at the apex, tachycardia, mild congestive heart failure as noted by enlargement of the liver and râles in the lung bases posteriorly, and clinical recovery within a few days. The electrocardiographic abnormalities persisted in this patient for a month. It is regrettable that we were unable to secure additional periodic observations on this patient.

Although too few cases of mumps myocarditis have been recognized to establish a clinical picture, it would appear that the myocarditis is nonspecific in nature and gives rise to symptoms and signs which differ in no respect from myocarditis from other causes. The exact incidence and the relation of this complication to the severity of the preceding parotitis are questions which remain unanswered. As Wendkos and Noll suggested, awareness of this condition may lead to increasing recognition. It seems plain, however, that cardiac surveys by all available methods of study should be undertaken on patients with mumps, and that the length of convalescence should be judged by the symptoms and findings of any cardiac disease, electrocardiographic studies, and periodic sedimentation rates.

SUMMARY

To our knowledge, this is the first case reported in the literature of myocarditis complicating mumps in which both clinical and electrocardiographic confirmation of the diagnosis could be made. No etiological cause for the myocarditis, other than mumps, could be determined.

REFERENCES

1. Wendkos, M. H., and Noll, J.: Myocarditis Caused by Epidemic Parotitis, AM. HEART J. 27: 414, 1944.
2. Pujol, M.: Mumps and Myocarditis, Arch. de méd. et pharm. mil. 69: 527, 1918.
3. Manca, C.: Myocarditis From Epidemic Parotitis, Arch. ital. di anat. e istol. pat. 10: 716, 1932.
4. Bruenn, H. G.: Mechanism of Impaired Auriculoventricular Conduction in Acute Rheumatic Fever, AM. HEART J. 13: 413, 1937.
5. Keith, J. D.: Overstimulation of Vagus Nerve in Rheumatic Fever, Quart. J. Med. 7: 29, 1938.
6. Wendkos, M. H., and Noll, J.: A Survey of Rheumatic Fever in a Large Station Hospital, M. Clin. North America 28: 124, 1944.

Abstracts and Reviews

Selected Abstracts

Bevans, M.: Changes in the Musculature of the Gastrointestinal Tract and in the Myocardium in Progressive Muscular Dystrophy. Arch. Path. 40: 225 (Oct.) 1945.

The author records the clinical and pathologic observations in four patients with progressive muscular dystrophy. In the voluntary muscles the changes were the recognized ones of progressive muscular dystrophy. While all four patients had myocardial lesions, only one patient showed in life clinical signs of heart failure, though all had tachycardia. The only electrocardiographic finding was right axis deviation, which two patients exhibited.

A composite picture of the gross myocardial lesions showed increase in, and opacity of, the myocardial fat, streaks of fibrosis throughout the myocardium, particularly the left ventricle, and slight focal thickening of the endocardium. Microscopic examination revealed a peculiar distribution of the scarring and of the areas of muscle degeneration. The most extensive lesions were seen near the epicardial surface, where the fibrous tissue which penetrated and replaced the myocardium appeared to be continuous with the epicardial fat or with the thickened epicardium. The myocardial fibers showed changes which were comparable to those seen in the skeletal muscles, although there were certain differences. Changes of a similar character were noted in various parts of the gastrointestinal tract.

BELLET.

Hiatt, E., Brown, D., Quinn, G., and Macduffie, K.: The Blocking Action of the Cinchona Alkaloids and Certain Related Compounds on the Cardioinhibitory Vagus Endings in the Dog. J. Pharmacol. & Exper. Therap. 85: 55 (Sept.) 1945.

The authors have determined and compared the plasma concentrations of certain cinchona alkaloids necessary to produce a blocking action on the cardio-inhibitory vagus endings in the heart of the dog. The alkaloids studied were quinine, quinidine, cinchonine, and cinchonidine. The conclusion of the authors is that of the alkaloids studied only quinidine effectively blocked the vagus endings at blood concentrations which, if applied to man, would not produce toxic effects. To effectively block the vagal endings it was necessary for quinine sulfate to reach a plasma concentration of 19.8 mg. per liter. The effective levels of cinchonidine and cinchonine sulfate were, respectively, 15.5 and 13.3 mg. per liter. Quinidine sulfate, on the other hand, was effective at an average plasma level of only 7.4 mg. per liter. The plasma levels of quinidine sulfate necessary for the successful treatment of auricular fibrillation and blocking the vagal endings are comparable.

BELLET.

Rappaport, A. E., Nixon, C. E., and Barker, W. A.: Fatal Thrombocytopenic Purpura Due to Sodium Salicylate. J. Lab. & Clin. Med. 30: 916 (Nov.) 1945.

A Negro man, 35 years of age, was given a total of 2,640 grains of sodium salicylate in thirty-three days. There were no untoward effects. After a drug-free period of fifteen days, the administration of sodium salicylate was resumed, and nine days later he showed the typical manifestations of thrombocytopenic purpura. Splenectomy failed to influence the hemorrhages. Further evidence of a toxic origin of the purpura consisted in the morphologic characteristics of the megakaryocytes and the metaplastic appearance of these elements in the spleen.

BELLET.

Barnes, Arlie R.: The Consideration of Two Cardiac Diseases Amenable to Surgical Treatment. Journal-Lancet 65: 382 (Nov.) 1945.

Barnes considers the minimal requirements for the diagnosis of patent ductus arteriosus to be, first, a continuous murmur (in the sense that there must be a diastolic as well as a systolic element), and second, roentgen evidence of some enlargement of the pulmonary conus. The diagnosis must be made with caution in the absence of an increased pulse pressure. McMILLAN.

Gaston, E. A., and Folsom, H.: Ligation of the Inferior Vena Cava for the Prevention of Pulmonary Embolism. New England J. Med. 233: 229 (Aug.) 1945.

Since venous thrombosis is a disease that frequently affects the vessels of both lower extremities ligation of the inferior vena cava seems desirable, since this procedure not only interrupts the venous channel above an evident femoroiliac thrombosis, but also acts to prevent embolism from a simultaneous subclinical phlebothrombosis that probably exists in the veins of the opposite lower leg. The authors report two cases in which ligation of the inferior vena cava was performed below the level of the renal veins. Although an operation of some magnitude, it is compatible with recovery in seriously ill patients. A consideration of the available collateral pathways for venous return around the point of ligation indicates that eventual return to a normal venous pressure relation should ensue.

The indications for ligation of the inferior vena cava are not well defined. A pretty clear indication is the occurrence of several pulmonary emboli secondary to peripheral venous thrombosis. A review of the literature is also included in this report. McM.

Segall, E. L., and Dorfman, W.: Death Following the Intravenous Administration of Papaverine Hydrochloride. New England J. Med. 233: 590 (Oct.) 1945.

Severe respiratory symptoms, hyperpnea, and tachypnea, developed in two patients within thirty seconds after the intravenous administration of papaverine. In both patients death occurred within five minutes. One patient, aged 80 years, had auricular fibrillation and, apparently, an embolism to the bifurcation of the aorta. The second patient, a 61-year-old woman, suffered from pulmonary embolism with infarction of the right lower lung lobe.

Since respiratory symptoms began so quickly, the authors feel justified in attributing death to the medication. McM.

Levine, Samuel A., and Hindle, J. A.: Coronary Artery Disease Among Physicians. New England J. Med. 233: 657 (Nov.), 1945.

Levine and Hindle have attempted to secure statistical data bearing on the widely held opinion that coronary artery disease occurs more frequently in professional men, particularly physicians, than in other groups. They felt that a comparison of the age at the time of death from coronary artery disease in different groups would more accurately answer this question than would a consideration of the number of reported deaths.

Using 66.3 years as the average age of physicians at the time of death from all causes, their analysis showed that 65.8 years was the average age at death from coronary artery disease both in physicians and in the general population. The difference was not significant. McM.

Drury, Alan N.: Observations Relating to Cardiac Hypertrophy Produced in the Rabbit by Arteriovenous Anastomosis, the Effect of Closure of the Anastomosis. Quart. J. Exper. Physiol. 33: 107 (May) 1945.

Drury carried out a series of studies on rabbits designed to show (1) whether the cardiac enlargement that develops after A-V anastomosis is the result mainly of hypertrophy or of dilatation and (2) whether or not this enlargement disappears after the A-V connection is abolished. From the experiments reported in this paper, as well as from earlier work, the author is satisfied that very real cardiac hypertrophy develops within six to eight weeks after

the establishment of an A-V anastomosis in rabbits. The hypertrophy disappears equally promptly after correction of the anastomosis. Only one animal showed any persistence of the hypertrophy. The author classifies hypertrophy which disappears as physiologic. The one example in which hypertrophy persisted after elimination of the A-V connection led the author to speculate as to whether physiologic hypertrophy may not become pathologic hypertrophy.

McMILLAN.

Burnett, C. H., Bland, E. F., and Beecher, H. K.: Electrocardiograms in Traumatic Shock in Man. J. Clin. Investigation 24: 687 (Sept.) 1945.

The authors hoped to obtain some information from electrocardiograms which would help to answer the question of whether the diminished cardiac output in shock is the result of cardiac involvement or is produced entirely by extracardiac factors. Thirty severely wounded soldiers were studied. Because of the conditions under which the studies were carried out and because many of the patients had chest wounds, chest leads were not made. Twenty-five of these thirty patients, all in marked and some in profound shock, showed no electrocardiographic changes. Some of the electrocardiographic abnormalities that were present in the remaining five patients are of interest. In two there was definite inversion of the T waves in Lead I, which disappeared within one hour after blood transfusion and a resulting rise of blood pressure. Both patients had wounds of the left chest but no evidence of actual cardiac or pericardial injury. Right axis deviation was anticipated as a result of the free use of fluids but was encountered only once. A fourth patient, who did not survive and may well have had some injury to the heart or pericardium, showed notched QRS complexes of low voltage in all leads. The fifth patient presented transient auricular fibrillation, with short runs of superimposed ventricular tachycardia. The conclusions to be drawn from this study are essentially negative and the authors emphasize as significant that twenty-five patients showed no electrocardiographic changes and only five exhibited any abnormality.

McMILLAN.

Rantz, L. A., Boisvert, P. J., and Spink, W. W.: Etiology and Pathogenesis of Rheumatic Fever. Arch. Int. Med. 76: 131 (Sept.) 1945.

The authors summarize four types of evidence which in the past twenty years have made it "increasingly apparent that infection by hemolytic streptococci is in some way related to the development of the rheumatic state." In their own series of 1,500 cases of respiratory infection they found 15 cases of rheumatic fever among 410 convalescents from streptococcal infections and no cases of rheumatic fever among the other 1,100 convalescents from nonstreptococcal infections.

The authors noted that among these patients rheumatic fever may follow streptococcal infection without any intervening latent period. In such patients, fever, fatigability, anorexia, weight loss, and persistent elevation of the sedimentation rate gave evidence of continued disease immediately following the frank streptococcal infection. During this period, many of these patients exhibited electrocardiographic changes including inversion of T waves and prolongation of the P-R interval. These electrocardiographic changes, however, were also found in some of the apparently normal convalescents from streptococcal disease.

In conclusion, a plea is made for the examination of rheumatic subjects for circulating antibodies or tissue hypersensitivity to streptococcal proteins in a more pure state than has been available heretofore.

T. N. HARRIS.

Rinehart, J. F.: Observations on the Treatment of Rheumatic Fever With Vitamin P. Ann. Rheumat. Dis. 5: 14 (Sept.) 1945.

The purpose of this paper is to report observations which were made on 39 cases of rheumatic fever which have been treated with vitamin P for one month or longer. Of the 39 patients, 24 were children and 15 were adults. All showed activity of the rheumatic process at the time treatment was instituted, and many were of the polycyclic or refractory type. The preparation used in most cases was crude hesperidin, 0.5 Gm., fortified with 20 mg. of hesperidin methyl chalcone. The usual dose was 1.5 Gm., one tablet, three times daily with

meals. No toxic or ill effect was noted. The vitamin P was given in all cases as additional therapy.

Twenty-six of the 39 patients had exhibited persistent rheumatic activity for six weeks or longer. One month after the institution of treatment, their sedimentation rate had fallen from an average of 33 mm. to 17.5 mm. per hour. Thirty-four patients exhibited significant slowing of the sedimentation rate by the end of six weeks. Twenty-two of the 39 patients showed either no evidence of activity or minimal activity after four to six weeks of therapy. These results, chiefly in terms of slowing sedimentation rate but paralleled by other clinical manifestations of improvement, are considered evidence that vitamin P exerted a beneficial influence on the course of the illness. LAPLACE.

Bedell, A. J.: Clinical Differentiation of Emboli in the Retinal Arteries From Endarteritis. Arch. Ophth. 34: 311 (Oct.) 1945.

This paper is a summation of the study and correlation of cases of sudden blindness caused by the abrupt closure of the central retinal artery or one of its branches, and its purpose is to facilitate the differentiation of embolism of the retinal artery from endarteritis. Illustrative case reports are presented. The diagnostic criteria for embolism of the central retinal artery, on the one hand, are contraction of the arteries to threadlike size, great reduction in size of the veins, frequent visibility of the wall of the artery, and retinal edema limited to an oval area. It is characteristic of retinal endarteritis, on the other hand, that the arteries are rarely as small as those found in cases of embolism, that there are always white plaques along their walls, and that the retinal edema involves the entire visible fundus. In both embolism and endarteritis, the optic nerve appears white, atrophic, and sharply outlined. LAPLACE.

Smithwick, R. M.: Experiences With the Surgical Treatment of Essential Hypertensive Cardiovascular Disease in Man. Cleveland Clin. Quart. 12: 105 (Oct.) 1945.

The operation employed by the author consists of a two-stage sympathectomy involving removal of sympathetic trunks from at least the tenth dorsal through the first lumbar, inclusive, at most from the sixth dorsal through the third lumbar, inclusive, and usually from the eighth dorsal through the first or second lumbar. In all cases the great splanchnic nerves are removed from the celiac ganglia to the mid-thoracic region, and divided rami are carefully clipped with silver dural clips to guard against regeneration. Postoperative postural hypotension is a valuable sign indicating that important pathways have not been overlooked, and its presence in cases where the operation fails makes it reasonably certain that inadequate surgery is not the explanation. Postural hypotension usually disappears in a few months.

In a six-year period, over 600 unselected patients were operated upon. The operative mortality was 2.2 per cent: 2 per cent within one year of operation and 3.6 per cent one or more years after operation. Nearly two-thirds of the deaths occurred in patients who had a resting diastolic pressure of 140 mm. or more, together with such manifestations as advanced eye ground changes, encephalopathy, and poor cardiac or renal function. Operation in such cases now seems very rarely advisable. The majority of a series of 179 unselected patients observed for a period of one to five years were improved. Beneficial effects included changes in the eye grounds, electrocardiogram, and cardiac and renal functions as well as subjective improvement. The diastolic pressure was lowered 30 mm. or more in 42 per cent of the cases, 20 to 29 mm. in 18 per cent, 10 to 19 mm. in 20 per cent, and 0 to 9 mm. in 12 per cent. In 8 per cent of the cases the blood pressure was higher. Studies are now in progress to determine criteria by which the outcome of operation may be anticipated. Results indicate, for example, that women are better subjects than men.

Among the patients who were operated upon, two were found to have pheochromocytoma. Both had severe hypertension of the narrow pulse pressure variety which was nonparoxysmal. Their blood pressure returned to normal and they have continued to do well for several years after operation. LAPLACE.

Groedel, F. M.: The Pneumocardiogram. Exper. Med. & Surg. 3: 361 (Nov.) 1945.

The author describes pneumocardiography as the technique of obtaining a record of the pressure changes within the thorax which are created by and which accompany each heartbeat. The literature is reviewed and the conclusion cited that there is no fundamental difference between the recorded curves of pressure (pneumocardiogram) and those of air velocity (pneumotachogram) as the typical points of inversion of the curves in both are found to be identical. The author's technique for recording the pneumocardiogam consists in utilizing an anesthesia mask, the outlet of which is directly connected with a microphone by 3 cm. of rubber tubing. The chief technical difficulty is that of teaching the patient to open his glottis while the record is being made.

The physiologic basis for the various deflections of the pneumocardiogram is still largely controversial, and further careful work on the subject is desirable. The author found, however, that the cardiopneumographic peaks can be very well timed and explained on the basis of the phlebogram. The cardiopneumogram was, in fact, found to be almost identical in normal cases with a phlebogram obtained by means of a receiver bell loaded with 300 grams. The conclusion is reached that both consist of air- and venous-blood tidal waves which represent the pressure changes in the thorax due to the blood in- and outflow, and of superimposed air- and venous-blood concussion waves which reflect the various mechanical events in the heart. LAPLACE.

Kottke, F. J., Kubicek, W. G., and Visscher, M. B.: The Production of Arterial Hypertension by Chronic Renal Artery-Nerve Stimulation. Am. J. Physiol. 145: 38 (Nov.) 1945.

Since reducing the blood flow to the kidneys by mechanical constriction of the renal arteries produces hypertension, it seemed desirable to ascertain whether decreasing renal blood flow by stimulation of renal vasoconstrictor nerves might likewise cause an elevation of blood pressure. The studies reported were carried out on dogs. Electrodes were placed around one or both renal arteries and their accompanying nerves. In the acute experiments, the dogs were anesthetized, the blood pressure was recorded directly, and the renal blood flow was estimated by a thermostromuhr. Electrical stimulation with various types and frequencies of current was effective in producing renal vasoconstriction. There was, however, no significant increase in arterial pressure, even with a 75 per cent reduction of renal blood flow for as long as two hours. In the chronic experiments, arterial pressure was recorded indirectly by employing a Van Leersum loop around the left carotid artery. Shielded unipolar silver electrodes were applied to each renal pedicle, using aseptic technique. The leads were brought out through a stab wound in the back, and the animal was allowed to recover. A sinusoidal alternating current of 2 c.p.s. was applied for twenty to twenty-two hours daily. This procedure was effective in producing arterial hypertension with pressures as high as 238/194, and, in one animal, a convulsive state associated with elevated blood creatinine. Hypertension was maintained for as long as twenty-seven days but subsided when the continuous stimulation was withdrawn.

There was no evidence that a persistent hypertension could be produced by the means described. On the basis of these studies, the authors state that hypertension of the type produced by chronic renal artery-nerve stimulation does not appear to be a simple hemodynamic consequence of renal vasoconstriction. LAPLACE.

Parkinson, John: The Harveian Oration on Rheumatic Fever and Rheumatic Heart Disease. Lancet 249: 657 (Nov.) 1945.

The first part of the oration deals mainly with the diagnosis of early rheumatic heart disease. Parkinson states that, whereas too much emphasis was once placed on systolic murmurs, the pendulum may now have swung too far in the other direction. Any fairly

obvious systolic murmur should be looked upon critically. Roentgenology is at present of great help in recognizing rheumatic heart disease in its early stages. No method of study, however, eliminates the necessity of basing one's decision as to whether a systolic murmur is organic or incidental mainly upon the quality of the murmur. "The louder, the longer and the more constant the murmur, the more likely it is to represent organic change." Many typical examples of mitral stenosis show only a systolic murmur, although there is nearly always associated roentgen evidence of some left auricular enlargement.

The second part of the oration is devoted to the "Problems of Rheumatic Fever." In Great Britain, 2.6 per cent of the child population of London are estimated to have had this disease, and probably 16,000 persons out of a population of forty million die of the disease and its sequelae yearly. Parkinson feels that rheumatic fever has the ability to produce immunity and subscribes to the view that a large proportion of the population have at one time had the disease in a minimal or subclinical form and are partially immune.

Concerning the etiological role of hemolytic streptococci, the author believes that "while there is some causal relation between the streptococcus and rheumatic fever, the streptococcus is not the essential cause." He is of the opinion that one cannot dismiss the possibility that some specific organism, at present unidentified, may prove to be the cause of rheumatic fever. A chief reason for this point of view is the almost specific involvement of the mitral valve by rheumatic fever, which is unlike the behavior of other known streptococcal diseases, particularly scarlet fever.

The debated question of the advisability of removing tonsils is discussed. Parkinson expresses the view that, if the tonsils are visibly infected and if the tonsillar glands are enlarged, they constitute a greater danger to rheumatic than to other children. McMILLAN.

Ben-Asher, S.: The Treatment of Anginal Syndrome With Thiouracil. J. M. Soc. New Jersey **42**: 401 (Dec.) 1945.

The benefit in cases of angina pectoris which is obtained by total thyroidectomy suggested that a similar result might be obtained by the administration of thiouracil. Such a result was actually observed by the author in 1943 in the course of treatment of a case of hyperthyroidism in which anginal pain subsided when thiouracil was successfully used in reducing the metabolism. Since then the author has employed thiouracil in the treatment of eight patients who had angina pectoris. Electrocardiographic abnormalities were present in all cases. The basal metabolism was slightly elevated in one case and normal in seven cases. Each patient was given 0.6 Gm. of thiouracil daily for two weeks, followed by a maintenance dose of 0.2 Gm. daily. No other medication was given except nitroglycerin for relief of pain during an attack. By the criterion of relief of pain in the course of ordinary daily activity, the author considers that the treatment was beneficial in all cases. The results are graded as excellent in two cases, good in five cases, and fair in one case. In all cases the basal metabolic rate was reduced to -8 to -20 per cent at the time of maximum improvement. In five cases improvement was maintained after thiouracil therapy was stopped, and in two cases a relapse occurred within six to eight weeks after changing from thiouracil to a placebo. The author emphasizes the fact that spontaneous improvement is common in the course of angina pectoris, but he believes that the results of thiouracil therapy are, nevertheless, sufficiently impressive to warrant further investigation of this form of treatment. LAPLACE.

Kinney, Thomas D., Sylvester, R. E., and Levine, S. A.: Coarctation and Acute Dissection of the Aorta Associated With Pregnancy. Am. J. M. Sc. **210**: 825 (Dec.) 1945.

The authors could find only two previously recorded instances of combined coarctation and dissection of the aorta. They report a third example which is the first case in which a complete diagnosis was made ante mortem. The diagnosis of coarctation was suggested chiefly by arterial pulsation in the back and the absence of palpable pulsation of the abdominal aorta and femoral arteries. The principal finding that suggested dissecting aneurysm was the

sudden onset of pain in the throat and upper back. An enlarging cardiac silhouette, demonstrated by roentgenogram and certain abnormalities in the electrocardiogram added further confirmation.

At necropsy changes in the aorta which were compatible with idiopathic medial cystic necrosis were present proximal to the coarctation, but were not present distal to the obstruction. Reports by other observers of this pathologic lesion in association with coarctation, both with and without dissection, are cited. McMILLAN.

Race, George A., and Lisa, James R.: Combined Acute Vascular Lesions of the Brain and Heart, A Clinical-Pathologic Study of Fifteen Cases. Am. J. M. Sc. 210: 732 (Dec.), 1945.

Race and Lisa analyzed the necropsy findings of one hundred consecutive patients in whom acute vascular lesions of either the brain or heart were present. In 15 patients both myocardial infarction and either diffuse petechial cortical hemorrhage or massive cerebral hemorrhage were found. They feel that this combined involvement is neither infrequent nor coincidental, and suggest that cerebral anoxia secondary to the myocardial infarction may well have been responsible for the cerebral lesions. In support of this view, they point out that five additional patients with myocardial infarction presented, in life, evidence of cerebral lesions, though no cerebral involvement was found at necropsy.

The clinical picture was confusing. In all instances the neurological findings predominated and were more constantly recognized. In eight of the 15 patients cardiac involvement was unsuspected during life. Slightly more than 50 per cent of the 20 patients died of bronchopneumonia. The authors suggest that sulfonamides be given prophylactically when combined cerebral and cardiac lesions exist. McMILLAN.

Sokolow, M., and Garland, L. H.: Cardiovascular Disturbances in Tsutsugamushi Disease. U. S. Nav. M. Bull. 45: 1054 (Dec.) 1945.

A study was made of 35 convalescent patients from the Southwest Pacific who had had tsutsugamushi disease three to six months previously. All of the patients had been ambulatory for a period of one to three months. The symptoms in all cases were strikingly similar and varied only in degree. The predominant symptoms were fatigability, weakness, dyspnea and palpitation on slight effort, and precordial pains. Dyspnea and palpitation were slight in approximately 60 per cent of cases, moderate in 30 per cent, and absent in 10 per cent. Examination of the heart involved occasional soft apical or pulmonic systolic murmurs but no evidence of valvular disease or pericarditis. There was no gross abnormality of the sounds and no evidence of congestive heart failure. A striking feature in one-third of the cases was vasomotor disturbance of the hands and feet, manifested by mottled coldness, clamminess, and acrocyanosis. The electrocardiogram was normal except for seven cases in which there were minor abnormalities such as slurred QRS complexes, low amplitude or flat T waves in Lead I, right axis deviation, and nodal and ventricular extrasystoles. The arm-to-tongue circulation time was normal in all cases. A few patients had minor decreases in vital capacity. However, the breath-holding tests were almost universally decreased, approximately 75 per cent of the patients failing to hold the breath for the normal time of forty-five seconds. Seven patients could not hold the breath longer than twenty seconds. A standard exercise test, consisting of twenty hops on each foot for a total of forty hops, was applied in 28 cases. The resultant dyspnea and palpitation were abnormal in 70 per cent of the cases and severe in 15 per cent. Blood pressure was normal, but two-thirds of the patients had abnormally rapid heart rates. X-ray examination revealed definite cardiac enlargement in four cases and questionable enlargement in two cases. Roentgenkymographic evidence of abnormal cardiac contractions was observed in 14 cases and consisted of slight to moderate "peaking" of ventricular waves in 14 cases, with shallow ventricular contractions in three cases. The course of the circulatory disturbances noted was progressively favorable,

and all of the men were able to proceed on furlough within ninety days prior to return to duty. Attention is called to the similarity of the convalescent circulatory manifestations of this disease and those reported for trench fever during World War I. LAPLACE.

Starr, I., and Mayock, R. L.: Convalescence From Surgical Procedures. I. Studies of the Circulation Lying and Standing, of Tremor, and of a Program of Bed Exercises and Early Rising. Am. J. M. Sc. 210: 701 (Dec.) 1945.

The purpose of this investigation was to search for objective abnormalities during convalescence from surgical procedures in order to explain why, during this period, patients do not feel as they do in health and are unable to perform certain tasks which in health would be easy for them. The studies employed included recording of pulse rate, blood pressure, and the ballistocardiogram, in both the horizontal and vertical positions. From the ballistocardiogram, the cardiac output was calculated and also an estimate made of the amount of tremor. Forty-four patients were studied in this manner before operation and during postoperative convalescence.

Twenty-five of the patients studied had been operated upon for hernia. They were in good physical condition before operation and the changes observed after operation could therefore be attributed to convalescence. These postoperative changes included, in the horizontal position, diminished cardiac output and late fall in blood pressure; and, in the vertical position, increased cardiac output and pulse rate and fall in systolic blood pressure. There was also an increase in the difference between the lying and standing pulse rate and the lying and standing cardiac output. The amount of tremor on standing was increased.

The remaining 19 patients studied had undergone more serious operations. They varied so much individually, according to the nature and severity of their illness, that averages of their results could not be considered significant. They showed, in general, the same trends as were found after herniorrhaphy, except where one of two factors entered into the situation. When large amounts of fluid were given intravenously, the usual postoperative fall of cardiac output was prevented and sometimes replaced by a rise. When the patient's ability to take food and fluids was improved by the operation (for example after gastrostomy for carcinoma of the pharynx), the postoperative course differed from the usual, and pulse rate, blood pressure, and cardiac output all tended to increase.

Ten of the patients operated upon for hernia were treated differently from the others. Beginning with the second postoperative day, they carried out a series of mild exercises. The patients lay in bed, exercised the arms and legs for five minutes, stood up for five minutes, then returned to bed and exercised again for five minutes. This procedure was repeated twice daily. These patients showed no significant difference from those who remained in bed, except that their blood pressure was slightly lower on the tenth day, at which time also the control group exhibited more tremor than the exercised patients, and three of them were unable to stand. The latter observations were indicative of better physical condition in the exercised patients, but the difference was apparent only on the one day. LAPLACE.

Starr, I., Mayock, R. L., and Battles, M. G.: Convalescence From Surgical Procedures. II. Studies of Various Physiological Responses to a Mild Exercise Test. Am. J. M. Sc. 210: 713 (Dec.) 1945.

The main purpose of this investigation was to answer the question as to whether or not the response to exercise is altered in postoperative convalescence. The authors speculated that during that period a given amount of work might be performed less efficiently than under normal circumstances. An easy weight-lifting test was designed which was carried out in the recumbent position and consisted in lifting a 10-pound iron bar from chest to arm's length thirty times in one minute. The subject breathed from a spirometer and the oxygen consumption and rate and volume of respiration were estimated before, during, and after the test. Pulse rate was counted and the ballistocardiogram was recorded. From the latter, estimates were made of cardiac output.

Tested in this manner, five healthy subjects exhibited, as reactions to exercise, an increase in oxygen consumption, respiratory volume, cardiac output, and heart rate, with a variable effect on respiratory rate. The work performed was approximately 600 foot pounds per minute and the mechanical efficiency averaged 12.7 per cent.

Twelve patients operated upon for hernia and eight operated upon for other causes, were tested in the same manner before and after operation. It could not be demonstrated that convalescence had any significant effect on the amount of oxygen consumed, the mechanical efficiency, the volume of respiration, the cardiac output, or the pulse rate during exercise. However, when attention was given to the duration of the changes induced by the exercise, the averages showed significant differences, the increased oxygen consumption, respiration, and pulse rate declining to a resting level more slowly during convalescence than before operation. These differences however, could only be demonstrated by the use of averages. It is pointed out that the variability of the responses of individual subjects is so great that there appears to be no possibility of designing a satisfactory test of the type employed in this study, for the detection of convalescence and its duration. LAPLACE.

Steiner, Sylvan A.: The Typical Headache of Essential Hypertension. Etiologic Considerations and Report of a New Form of Therapy. M. Ann. District of Columbia **14**: 531 (Dec.) 1945.

The author points out that there is an abundance of evidence that the "typical" headache of essential hypertension may be of psychogenic origin and possibly may not be produced by the elevated arterial tension per se. Hypertensive headache bears a striking resemblance to migraine, and the apparent relationship between the two suggested the use of ergotamine therapy for hypertension. In addition, because hypertensive headache usually occurs during sleep in the horizontal position, it was decided to investigate the effect of sleeping in a bed, the headposts of which were raised on 10-inch blocks. Twelve cases of hypertension with headache in which treatment involved elevation of the head of the bed, were reported. The patients had previously used nicotinic acid, phenobarbital, thyocyanates, and other medication without relief. Sleeping in the tilted bed, however, gave dramatic relief in ten of the twelve cases. One patient was considered a partial failure, being unable to sleep with more than a 5-inch elevation of the head of the bed. Four patients required oral ergotamine therapy and obtained complete relief after a week's course of medication.

LAPLACE.

Wedum, B. G., Wedum, A. G., and Beaghler, A. L.: Prevalence of Rheumatic Heart Disease in Denver School Children. Am. J. Pub. Health **35**: 1271 (Dec.) 1945.

Rheumatic heart disease is now the first cause of death, excepting accidents, among children aged 10 to 14 years, in Colorado as well as in the entire United States. Denver had the second highest death rate from rheumatic heart disease in children aged 5 to 14 years among the 25 largest cities in the United States during 1939 and 1940. Among children in Denver there has been no apparent decrease in the incidence of rheumatic fever. In connection with the activities of the Denver Area Rheumatic Fever Diagnostic Service, the authors undertook a study in which they personally examined 1,845 Denver high school girls. In this group a diagnosis of rheumatic heart disease was established in 1.63 per cent. In contrast with the incidence of rheumatic heart disease which was found by the authors, an incidence of only 0.48 per cent was reported when a series of 1,318 Denver school children was examined routinely by school physicians. The authors suggest, therefore, that public health officers, in all except the climatically favored southern part of the United States, should revise their conception of the amount of rheumatic heart disease in school children and regard it as 15 to 40 cases per 1,000 rather than 2 to 15.

The authors consider that the incidence of rheumatic heart disease and rheumatic fever in Denver is not disproportionately high as compared with other large northern cities, but it appears possible that the disease itself may be relatively more severe. LAPLACE.

Book Reviews

THE CARDIO-PULMONAL FUNCTION DURING PREGNANCY. By Gerhard Widlund, University Clinic of Obstetrics and Gynecology, Upsala Sweden, 1945. Privately printed, 125 pages.

In studying many simple cardiorespiratory functions during pregnancy, it has repeatedly been found that many of them present so marked variations that it was difficult to establish definite trends as the effect of pregnancy.

The present work is a painstaking, statistical study of oxygen consumption, ventilation, blood pressure, and heart rate in pregnancy, and of the response of pregnant women to work tests. The study includes a critical survey of the important literature on the subject.

The author has performed 488 examinations on 157 women after rest and after graded exercises; for controls he used 60 healthy nonpregnant women of childbearing age.

He confirmed the generally accepted increase in oxygen consumption as pregnancy advances. This was associated with an increase in ventilation through increase in respiratory depth. There was also an increase in vital capacity, but not commensurate with the increase in respiratory depth; consequently, the "functional elasticity" with respect to ventilation depth was diminished.

He verified a slight increase in systolic and diastolic blood pressure and definite increase in heart rate toward the end of pregnancy. The difference between the heart rate when lying down and when standing up is diminished during pregnancy and increased in the puerperium. The reason for this difference is discussed. The oxygen consumption per work-time unit for a given amount of work was the same in pregnant and nonpregnant women, except on severe effort which was accomplished less economically by pregnant women.

The author finally concluded that, in regard to all investigated functions, a pregnant woman at rest behaves similarly to a nonpregnant woman doing moderate work; that is, already at rest, she partly utilizes her reserves.

The work is a creditable contribution to a fundamental but neglected problem.

JULIUS JENSEN, M.D.

American Heart Association, Inc.

1790 Broadway at 58th Street, New York, N. Y.

THE American Heart Association is the only national organization devoted to educational work relating to diseases of the heart. Its activities are under the control and guidance of a Board of Directors composed of thirty eminent physicians who represent every portion of the country.

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